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Relationship between Trace Elements Levels and Lung Cancer Patients in Southern Iraq

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background: Our life relies on our ability to use all sorts of materials, like trace elements, in the world for our needs. The using of heavy metals has greatly contributed to the comfort of our everyday lives. Blood is directly affected by poisoning when such metals are inhaled from environments where heavy metals occur in high levels. Research is constantly advancing our knowledge of the connection between various trace elements and disease, particularly cancer, since the effects of heavy metals on human health remain a serious health concern.
Objective: The objective of this work is to establish levels of a range of elements in human blood, serum and hair samples of patient undergo lung cancer comparing with control (healthy persons) so that potential exposures can be better identified in future cases.
Methods: Elements concentrations including As(arsenic), Ba(barium), Co(cobalt), Li(lithium), Mg(magnesium), Mn(manganese), Mo(molybdenum), Rb(rubidium), Sr(strontium) and Ti(titanium) was analysis used MS ICP (an inductively coupled plasma atomic absorption spectrophotometer).
Results: Test found that Mn has substantially ($p<0.05$) high concentration in three tissues including whole blood, serum, and hair of patients with lung cancer (291,487.2,68.03) ug / l respectively. In comparison as occurs in the lowest concentration. Sr was 77.5ug / l, Rb 41.6ug / l, and Ba 35.2ug / g. On other hand, Co, Li, Mg, Mo and Ti were found in low levels ranged 1.7-5.5 ug/l, in whole blood of patients. Hair samples accumulated the lowest concentration of As, Ba, Co, Mg, Mn and Rb. When we compare the concentration of trace elements between lung patients and control samples, that clear most of the elements accumulate at high levels in lung cancer patients. Result found significantly high As, Ba, Co, Mg, Mo concentration in whole blood and serum of lung cancer

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patients, in contract, Li, Mn and Rb occur in high levels in whole blood of control sample. Even as hair of control samples have elevated levels of As, Sr and Ti. However, concentrations of trace elements in the whole blood of smokers and non-smokers showed that all ten elements accumulated at elevated levels in the blood of smokers relative to non-smokers. Spearman correlation found significantly positive correlation among trace elements in the blood of patients with smoker lung cancer and non-smokers.

Conclusion: The study conclude that trace metals level in smokers persons are elevated than non-smokers. The findings of this study lend some support to the link between heavy metals pollution and lung cancer cases.

Keywords: Heavy metals; lung cancer; levels; patient.

1. INTRODUCTION

Metals exposure causes illnesses and health conditions. It has been established that a number of human diseases are caused by the heavy metals. These diseases arise from unintentional exposure, whether from internal or external mechanisms. The emergence of various tumors is one of the serious health issues linked to heavy metal exposure. Exposure to heavy metals in the form of industrial-based carcinogens, cigarette smoke, and diet-related exposure to foodstuffs are the main risk factors for getting cancer [1]. Measuring potential health hazards in occupational individuals is difficult. So it's necessary to detect these metals in blood and other tissues. Even low trace element intake can cause health problems amongst individuals [1]. Lung cancer is among the most dangerous tumors that endanger human life; as the world's leading causes of death from cancer.

Several studies were found relationship between certain heavy metals and cancer development, Arsenic, cadmium, chromium, and nickel are classified as category one carcinogens by the International Cancer Research Agency and are applied industrially. Although a few metals, including copper (Cu) and zinc (Zn), are important intracellular enzymes and have a DNA-binding domain [2]. Prior researches has shown that smoking habit, family background as well as other factors like air pollutants impact lung cancer considerably [3]. However, Smoking is one of the leading cancer risk causes, contributing a significant proportions of the burden of lung cancer, particularly amongst men. Lung cancer risk is correlated with contamination particulates and cigarette smoke, which include metals which are carcinogens to the human lung. previous study by [4] reported serum levels of Pb, Fe, and Cu was higher in cancer group compared with control in darbandikhan north of Iraq [5]. Found The levels of nine metals like Mg, P, K Zn, Cu, Se, Rb, and Tl in tumor samples were substantially higher than their associated normal lung tissue, while further elements like Fe, Cr, Na and Cd showed reduced cancer sample concentrations relative to normal lung tissue equivalents. As well, High levels of Cu, Mn, Ni, and Cr have been shown to potentially cause lung cancer [6].

Arsenic is a toxic product, and there are significant risks to public health from exposures to this metal. As contact is usually a result of polluted food and water ingestion, environmental contamination evidence sturdily support arsenic's function in developing lung and bladder cancer [7,8]. Aluminum exposed in the breast tissue was being positively linked with carcinogenesis [9,10]. Cadmium exposure was associated with cancer in several tissues including breast, stomach digestive tract, prostate, lungs and tests. Cadmium also has a suggested role in developing of bladder cancer [11,12]. Nickel exposure has been associated with a variety of cancers. Epidemiological research showed a strong association between exposure and carcinogenic occurrence in the lungs, respiratory and sinus tissue [13,14]. Numerous reports have shown that exposure to heavy metals contributes to tumor suppressor gene expression derangement, remediation mechanisms, and metabolism-related enzymatic activity through oxidative damage [15,16].

Basrah is a large industrial city,about 450km southern of Baghdad, It suffered a great deal from war emissions, in addition to oil extraction and natural gas burning, all this condition lead to increased cancer case last years in this area. Cancers as well as congenital anomalies are amongst diseases whose threat is increased as a result of this contamination in this area. The objective of this assessment is to examine the concentration of heavy metals and trace elements including As, Ba, Co, Li,Mg, Mn, Mo, Rb, Sr, and Ti in three tissue specimens that inclusive whole blood, serum and hair of lung cancer patients to determine the association between metal levels and cancer progress.

2. MATERIALS AND METHODS

2.1 Reagents and Apparatus

30per cent (w / v) high-purity hydrogen peroxide and (W / V), Nitric acid grade of analytical reagent70 percent. Inductive coupled plasma mass spectrometry (ICP/MS) NexION 300D, the system manufactured by Perkin Elmer, New York, USA.

2.2 Samples Collection

from of Basrah Hospital has collected cases of lung cancer from the oncology center after achieving approval. Where approximately 30 patients with lung cancer, blood, serum and hair were sampled. Personal data from each case was obtained. The entire blood, serum and hair samples were collected for six months in 2019. The patients were males between 50 and 70 years old. Relevant information on smoking habits and social status were obtained from each patient. The comparison group was collected from 30 person, healthy, non-chronic disease individuals, their age ranging from 50-60 years old.

2.3 Experiment

Blood samples were taken from pulmonary patients cancer and control group. From every single individual, 5 ml of blood was squeezed using vein puncture Syringes which can be disposed of. The blood sample was inserted into Plastic disposable tube, then left in the room temperature within 20-30 min. Serum have been detached Clotted blood for 10 min by centrifugation.Hair sample take 0.5gm of patient and control after have permission, the hair was watching with acetone and de-ionized water alternatively, all samples were digested by add nitric acid and peroxide hydrogen as 2:1 then putting at hot plate until polling and the solution become clear. To complete the volume to 25 ml, water De-ionized water was then applied, otherwise the solution was filtered using filter paper N0.1. Samples were set in 50ml plastic container tubes for analyzation Inductive coupled plasma mass spectrometry (ICP/MS) NexION 300D. Each analysis was conducted in duplicate; standard and blank samples were analyzed with samples.

2.4 Ethical Consideration

We have ethical approval from the director of the Human Development Center at the Basra Health Department Issue 490,3 sep.2019.

2.5 Statistical Analysis

Statistical analysis was performed using the computer program Statistical Package for Social Sciences (SPSS) version 20.0 for Windows (IBM)SPSS Software for Statistics, IBM Corporation, New York, USA). One-way variance test was used to estimate the mean differences between three sample groups. The values for the result were conveyed as Mean ± SD and t-test was used to compare between patient group and control group with 95% Confidence Interval of the Difference. 2 replicates were obtained per sample, the study used a mixed effect model to compensate for correlation and to model cross-sample variation via random effect. spearman correlation(Correlation is significant at the 0.05 level (2-tailed) and at the 0.01 level (2-tailed). used to detect correlation among metals concentrations in the tissues.

3. RESULTS

3.1 Concentration of Trace Elements in Blood, Serum and Hair Sample of Lung Cancer Patients

This research was carried out to determine the values of ten trace elements in three biological samples of lung cancer patients. Table 1 show the Concentrations of As, Ba, Co, Li, Mg, Mn, Mo, Rb, Sr and Ti were detected in three tissues including blood, serum and hair in patients with lung cancer,and control (healthy persons). In whole blood of lung cancer patients the maximum value is Mn(manganese) reached 291 ug/l while the minimum level of As(arsenic) reported 1.48 ug/l. However, Sr is 77.5ug/l followed by Rb 41.6ug/l and Ba 35.2ug/g. While, Co, Li, Mg, Mo and Ti were found in low concentrations ranged 1.7-5.5 ug/l.

Concentration of Mn, Sr and Ba in serum was significantly ($p<0.05$) high compare with their levels in whole blood, whereas Co, Li and Rb (0.29, 4.1, 5.1 ug/L respectively) had the lowest serum values than whole blood (Table 1,Fig. 1).

Hair samples of lung cancer patient was accumulated low level of these metals, such as Arsenic found in 0.59 ug / L, Co, Mg, Mo, Rb and Ti (0.66,1.66.1.46.3.6 and 3.53) ug/l respectively, compared with their levels in whole blood and serum, the maximum concentration was record for Strontium 74.7ug / L (Table 1, Fig. 1).

3.2 Compare Concentration of Trace Elements between Lung Cancer Patients and Control

Fig. 2 clarifies the concentration of metals in patients with lung cancer(whole blood, serum and hair) as compared with control, arsenic detected at high concentration in control samples hair(2.8 ug/l) than hair of patients(0.59ug/l), while it exists at low levels in whole blood and serum control sample(1.16,0.186 ug/l respectively) (Fig. 2, A). Ba is present in the patient serum at a high level (48.13ug / l) than the control sample but there is no distinction between them depending on the whole blood and hair sample. Cobalt has a slightly higher concentration (3.33ug/l) in patient whole blood. quite the opposite, lithium found at high levels in whole blood control sample(9.833ug/l) than patient samples (Fig. 2,c,d).Magnesium and manganese reported higher levels in serum of patient (3.93,467.2 ug/l respectively) comparing with control samples(Fig. 2,E,F). Molybdenum had a high concentration compared to control in whole blood, serum and patient hair(1.70,2.56, and 1.46ug / l respectively). Whereas rubidium had a limited degree in whole blood sample of control (54.16 ug / l), in patients at 41.66 ug / l (Fig. 2,G, H). Concentrations of strontium and titanium in control hair samples (131.7,6.0 ug / l) is higher than their concentration in patients with lung cancer, other than the high concentration of St in whole blood and serum samples of patients with lung cancer (77.53,111.23ug / l) (Fig. 2,I, J).

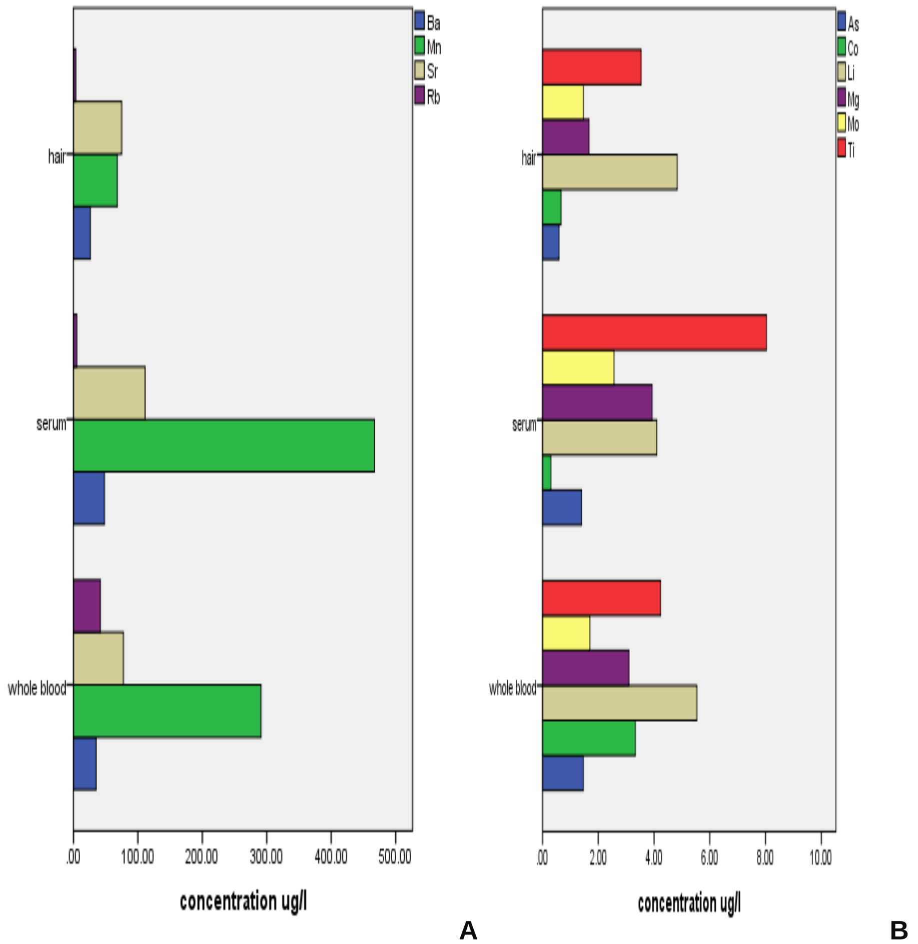


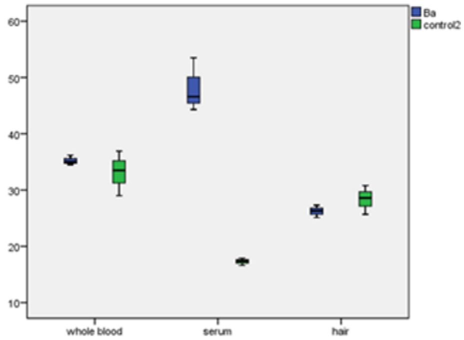
Fig. 1. Concentration of trace elements in whole blood, serum and hair of lung cancer patients, A: As, Co, Li, Mg, Mo, Ti, B:Ba, Mn, Sr, Rb

Table 1. Concentration of trace elements (ug/l) in whole blood, serum and hair of lung cancer patients, values mean ±SD.

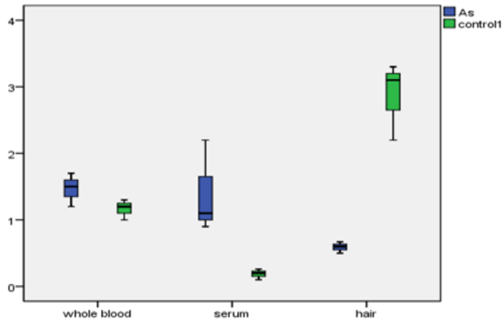
Trace elements		As	Ba	Co	Li	Mg	Mn	Mo	Rb	Sr	Ti
Whole	Mean	1.4667	35.2333	3.3333	5.5333	3.1000	291.0667	1.7000	41.6667	77.5333	4.2333
Blood	Std. Deviation	.25166	.87369	.73711	1.30512	.30000	83.05428	.26458	8.40972	9.70275	1.05987
Serum	Mean	1.4000	48.1333	.2967	4.1000	3.9333	467.2000	2.5667	5.1333	111.2333	8.0333
	Std. Deviation	.70000	4.78783	.09504	.55678	.66583	34.85570	.20817	.55076	51.06196	2.00083
Hair	Mean	.5900	26.2333	.6667	4.8333	1.6667	68.0333	1.4667	3.6333	74.7333	3.5333
	Std. Deviation	.08544	1.10151	.15275	.23094	.15275	2.68390	.35119	.20817	3.84231	.25166

Table 2. Concentration of trace elements (ug/l) in whole blood, of lung cancer patients (smoker and nonsmoker), values mean ±SD

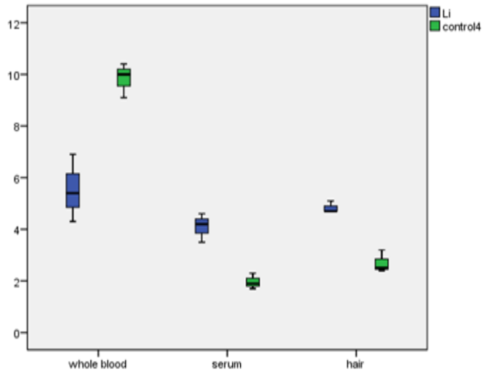
Trace elements		As	Ba	Co	Li	Mg	Mn	Mo	Rb	Sr	Ti
Smoker	Mean	1.3000	36.4333	3.0333	6.5667	3.4333	321.6667	1.6333	40.8333	77.4333	4.4333
	Std. Deviation	.10000	1.16762	.60277	1.04083	.70946	79.34944	.20817	7.46615	10.05004	.96090
Nonsmoker	Mean	.1667	8.6667	.2567	1.5333	1.9267	105.5667	.1467	21.7667	43.7667	2.6667
	Std. Deviation	.04509	.63509	.14572	.15275	.39107	33.10609	.03055	1.65025	1.71561	.40415


Ba
control2
whole blood
serum
hair

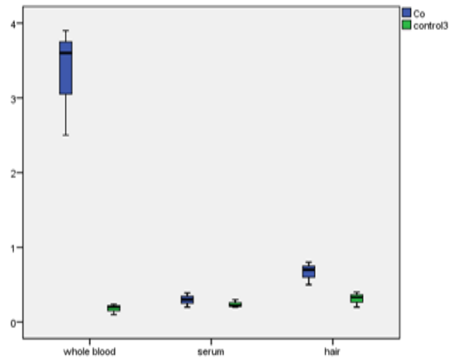
A


As
control1
whole blood
serum
hair

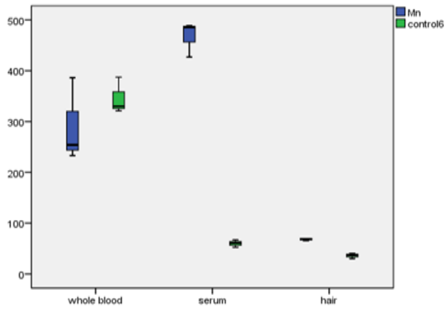
B


Li
control4
whole blood
serum
hair

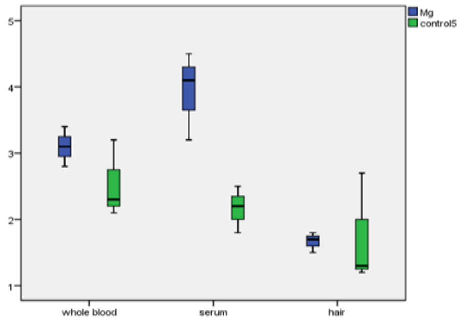
C


Co
control3
whole blood
serum
hair

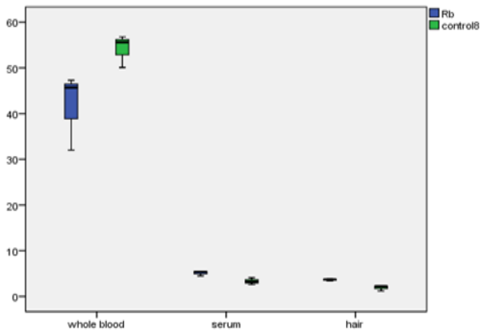
D


Mn
control6
whole blood
serum
hair

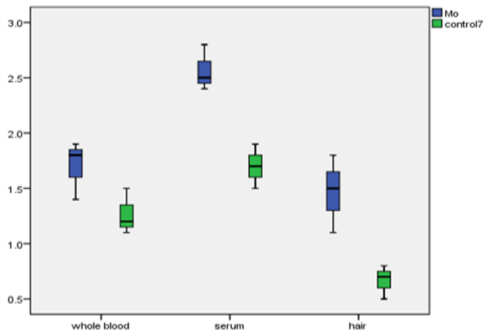
E


Mg
control5
whole blood
serum
hair

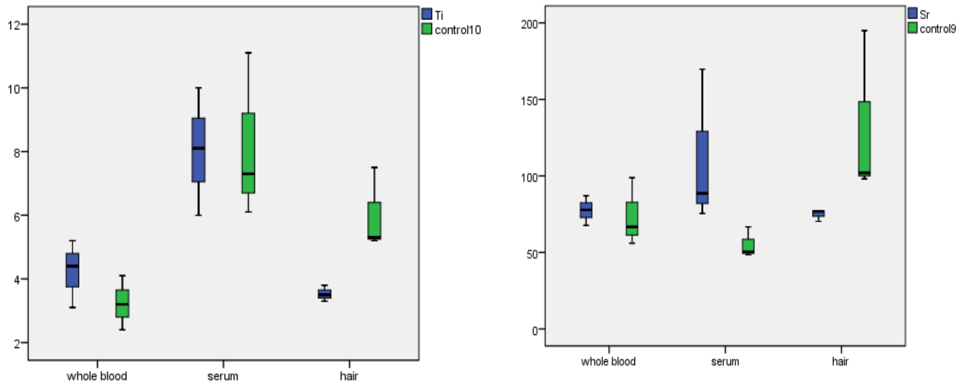
F


Rb
control8
whole blood
serum
hair

G


Mo
control7
whole blood
serum
hair

H



I J

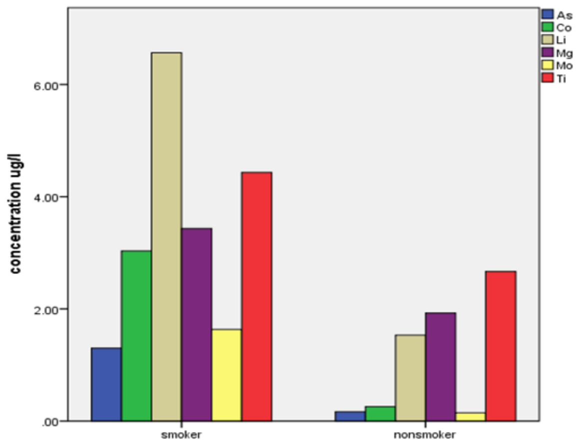
Fig. 2. Compare levels of trace elements(ug/L) between lung cancer patients and control(healthy persons)in whole blood, serum and hair, A:As, B:Ba, C:Co, D:Li, E:Mg, F:Mn, G:Mo,H: Rb, I:Sr, J:Ti

3.3 Concentration of Trace Elements in Smokers and Non-smoker Blood

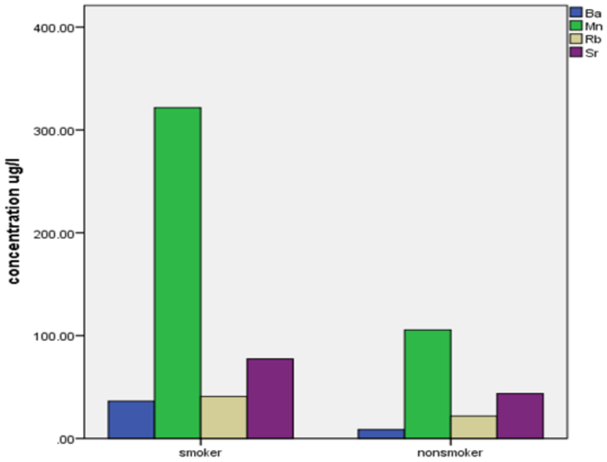
Table 2 and Fig. 3,A, B indicates the amounts of metals in smokers blood and non-smokers blood, resulting in all ten elements occurring at elevated rates in smoker's blood relative to non-smokers. Spearman correlation Table 3,found significantly positive correlation between trace elements in the blood of patients with lung cancer smokers and non-smokers.positive association between As-mg, As-Sr (r=0.94). The Ba-Co, Ba-Li correlation coefficient is 0.81,0.92.Mn and Mo, Rb (r=0.88).Mn and As(r=0.92) Table 3.

Table 3. Spearman correlation (2 tiled) among trace element in blood of smoker and non smoker patients with lung cancer

As	1	.841*	.714	0.771	0.771	.943**	0.771	0.771	.943**	0.543
Ba	.841*	1.000*	.812*	.928**	.812*	.928**	.841*	.841*	0.754	0.725
Co	0.714	.812*	1.000*	.943**	0.6	0.771	0.6	0.6	0.6	.829*
Li	0.771	.928**	.943**	1.000*	0.714	.829*	0.657	0.657	0.657	0.771
Mg	0.771	.812*	0.6	0.714	1.000*	0.714	.886*	.886*	.886*	0.771
Mn	.943**	.928**	0.771	.829*	0.714	1.000*	.829*	.829*	.829*	0.6
Mo	0.771	.841*	0.6	0.657	.886*	.829*	1.000*	1.000**	.829*	0.771
Rb	0.771	.841*	0.6	0.657	.886*	.829*	1.000**	1.000*	.829*	0.771
Sr	.943**	0.754	0.6	0.657	.886*	.829*	.829*	.829*	1.000*	0.6
Ti	0.543	0.725	.829*	0.771	0.771	0.6	0.771	0.771	0.6	1.000*



A



B

Fig. 3A, B. Concentrations of trace elements (ug / L) in lung cancer patients who are smokers and non-smokers

4. DISCUSSION

Study findings indicate that measuring the concentrations of trace elements in both lung cancer patients and normal cases is important in order to gain insight into the functions of these elements in carcinogenesis and therapeutic strategies in order to normalize the elements to be treated. The cause of cancer growth may be associated with an abnormally high concentration of certain metals [7].

Present study detected certain elements have high concentration in patients with lung cancer, in contract other elements occur in low concentration. Manganese is an essential component needed to health in small quantities but gradually becomes harmful expositions. Serum Mn in current study was substantially higher in patients with lung cancer, among the ten trace elements (Table 1), comparable to [18] and [7] it was in similar. Other research performed in China [18,19] find substantially lower rates of Mn among patients with breast cancer.

Mg is an important factor that plays a crucial role in various cellular reaction and in a range of metabolic and physiological activities Such as the synthesis of DNA and RNA and of proteins, There is proof that deficiency in Mg can cause types cancers (Andrea 2013). Mean concentration of Mg in serum of lung cancer patients is 3.93 ug/l, this is lowest compare with Al-Fartusie [6] et al (2017) he report 10.16 ug/g in serum of lung cancer patients. Smokers have high level of Mg than nonsmoker in this study. The key explanation for the low level of Mg that has been observed can be due to the involvement of Mg in the antioxidant protection mechanism by the activity of glutathione peroxidase, the enzyme that is responsible for the glutathione reaction and Freelance Radicals [20].

Present study find Sr exit in high concentration in whole blood and serum of patient, same found by (Zaichick and Zaichick [21]. They suggested high levels of Sr and Zn that trigger and promote prostate cancer through oxidative DNA damage, which is caused by an increase in free radicals generation and a decrease in the cell's antioxidant protection capability.Variations in concentrations of trace elements between different populations may indicate geographical location, cultural traditions, pollution or differences in composition and genetics of the body [22].

The current research showed that all ten elements in the blood of smoker patients with lung cancer accumulated at high levels than non-smokers, the same result stated by [23]. However, this finding agreement was reached with the previous study by [24] which recorded high levels of Cd, As, Zn in prostate cancer smokers. Smoking was one of the major intake sources for toxic elements, while smoking causes cadmium, arsenic, mercury, nickel and mercury inhalation [25,26].

Trace elements, while present in very minute quantities, play a very important role in human health. The rise in heavy metals results in increased oxidative stress, which is correlated with higher cancer risk([27]). For patients with diabetes and heart disease, elevated levels of Arsenic cause damage to the nerve cells and blood vessels. Taking smoking can in some circumstances lead to cancer due to various mechanisms such as genetic diversity and carcinogenic effects [28]). Result detected high concentration of Mg, Mo and Rb in whole blood, and lung cancer patient serum than control sample, this finding in contrast with [18] finding them decreasing in lung cancer patient plasma. Although it was close with increased concentration of Mn, Co, and Ba.

Heavy metal toxicity can cause everything from minor illnesses to serious diseases like cancer. Both have the potential to harm people's overall health. It is a fact that both occupational and environmental exposure are frequently linked to the main pathway causing human exposure. Comparable investigations have shown that, when tested against non-heavy metal exposure in tissue from controls, malignant tissue included greater levels of heavy metals such arsenic, aluminum, cadmium, lead, and nickel. Limiting human exposure to heavy metals is therefore a wise public health measure [29].

Despite these limitations, this is the only study we know in this region that metal levels has been checked in cases of lung cancer taking into account the smoking status. This work gives background knowledge for further analysis of the trace elements in etiology of lung cancer. Further studies are needed to determine the concentrations of heavy metals in other types of cancerous diseases, in different ecological regions, and in different age groups for the purpose of further investigation.

5. CONCLUSION

We studied the whole blood, serum, and hair levels of multiple trace elements in patients with lung cancer and control subjects, and for the first time we compared the concentration of trace elements between smokers and non-smokers who experience lung cancer. The high value in whole blood of patients with lung cancer is Mn while the minimum amount is As. Hair samples of lung cancer patients were accumulated low comprehensive levels of metals than other tissues. levels of As, Rb, Sr and Ti were high in control sample hair, while Li had high concentrations of control samples in whole blood. The study shows that trace metals concentrations in smokers are much higher than non-smokers. Several areas of attention for future work have been made clear by the research to this point. It is obvious that a thorough understanding of cancer-causing processes is required. This could lead to the development of individualized therapeutic or preventative strategies for particular heavy metals. Effective educational initiatives are also required in high-risk regions to increase public knowledge of the dangers of heavy metal exposure.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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