Article

Levels of Chromium as a biomarker for detection of Lung Cancer

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Abstract

The current study focused on estimating the level of chromium in biological tissues such as nails using inductively coupled plasma-atomic emission spectroscopy (ICP-AES) technology, as this technique is distinguished by its ability to estimate small amounts of chromium up to 0.005ppm. A several parameters were used in this study such as age, gender, as well as a comparison between people who smoke and non-smokers to estimate the level of chromium. 122 samples were collected and divided into two parts, including 55 models for people with lung cancer and 67 models for healthy people. The results showed a high percentage of chromium in people with lung cancer (0.2757 ± 0.0209 mg/kg). Compared to healthy people (0.0437 ± 0.0044 mg/kg). The study found that one of the causes of high levels of chromium in lung cancer patients is due to smoking, as the percentage of chromium in affected smokers reached (0.2665 ± 0.0262 mg/kg) compared to non-smokers (0.0875 ± 0.0103 mg/kg). A comparison was also made between the percentage of chromium in infected men and women. The study found a higher percentage of chromium in men (0.2230 ± 0.02050 mg/kg) in comparison to females (0.0646 ± 0.00987 mg/kg) because men are more addicted to smoking than women. In this study, a statistical analysis program was used SPSS at $P < 0.05$).

Keywords: Human fingernails, Lung cancer; Chromium, ICP-AES.

Introduction

Lung cancer represents a major cause of cancer-related mortality, which accounts 12 percent of cancer identifies but 20 percent of cancer fatalities [1].There is owing, in part, to a lack of adequate screening, in addition to the late onset of symptoms. As a result, the majority of patients will have advanced cancer and show incomplete responses to immune, radio, and chemotherapy. Considering absence of a viable treatment for people with disseminated disease, there is a growing interest in chemoprevention, especially attempts to restrict exposure to recognized lung cancer risk variables [2]. Heavy metals like (Cr), (Al), (Cd), and (Pb) can enter the human body from a variety of sources, such as water, soil, fresh and processed food, beverages, fish, detergents, paint, cosmetics, dairy products, and other commonplace goods [3], [4].Many businesses commonly discharge Cr into water resources, including the textile industry, the tannery, the manufacturing of dyes for painting and wood protection goods, electrolysis, metal coating, and chromate synthesis [5]. Hexavalent chromium [Cr(VI)] is a little-known industrial carcinogen. Cr(VI) is a metal ion that is frequently applied to materials in order to improve durability and resistance to corrosion, and it is widely utilized in manufacture. Welders are especially vulnerable to occupational exposure because chromium in stainless steel oxidizes at high temperatures to the Cr(VI) form, which is possibly ingested or exhaled in fumes. Over time, Cr (VI) may accumulate in bronchial epithelium. Though they can reduce it, protective equipment and/or fume extractors cannot totally eliminate Cr (VI) inhalation, and in some manufacturing industries, exposure to Cr (VI) poses a risk to workers. Though association between lung cancer risk and Cr (VI) exposure is widely established, the mechanisms by which Cr (VI) promotes lung tumor genesis remain unknown. According to recent data, intracellular processes convert Cr (VI) to Cr (III) becomes stuck inside cells and causes a rise in reactive oxygen species (ROS) .It has been claimed that this increase in ROS causes genetic instability, resulting in development of lung cancer. Despite this being a conceivable method by which Cr(VI) promotes or accelerates tumor formation, the downstream effects of Cr(VI) on tumor-permissive cell signaling events remain largely unknown [6]. Vital organs such as the liver, kidneys, respiratory system, circulatory system, and central nervous system are known to suffer detrimental effects from heavy metal intoxication. Serum count decline, non-melanocytic skin cancer, malignant melanoma, allergies, lung conditions, and degenerative neurologic illnesses can all be brought on by long-term exposure to heavy metals. Therefore, it is essential to measure metal concentrations to track and assess the effects of exposure on health, especially in individuals who are highly

exposed. Measurements of the heavy metal concentrations in the blood, serum, urine, hair, fingernails, saliva, and other tissues of the exposed group are frequently performed to assess exposure. Nails provide a trustworthy measure of body metal levels, unlike blood and other biological fluids. The growth rate of toenails is 0.05-1.2 mm/week, however they grow 30-50% slower than regular nails, which gives metals more opportunity to integrate. They are an ideal tool for screening and diagnosis since they are easy to gather, transport, and store, and their analysis is simple [7]. Over time, toxic components are absorbed into longer-term biomarkers like nails, which are excretory systems that can record exposures from both occupational and environmental sources. Because of its low level of external contamination, long retention period (two to twelve months), and absence of element level variation brought on by shifting bodily metabolic processes, human nails make excellent biological samples. [8].The objectives of this research include assessing the scientific knowledge on the carcinogenic effects of chromium (Cr) and to establishing whether there is currently enough evidence to suggest a relationship between chromium levels in nails and lung cancer.

Samples collections and preparation

Fingernails

Fingernails tests were gathered from hand or foot nails for all people, under 0.5 g from the fingernails utilizing (CH3)2CO/refined deionized water washed. This treatment was embraced to forestall sullying presented by device amid test gathering. For the most part, an example (mass more than 0.5 g) was gathered & put away in a polyethylene (PE) sack at $25C^0$ while waiting for the season of examination [9, 10]. Fingernails utilizing CH3)2CO/refined deionized water washed nail clippers in order to type the example more identically [10].

Washed and digestion for fingernail

In a nutshell, the cut Fingernail test was washed utilizing consecutive washing method (CH3)2CO- H2O- H2O - H2O – (CH3)2CO) was used in this investigation [9]. Tests were dried in a broiler medium-term at 60ºC at that point and put away at 25 ^oC in named polyethylene (PE) sacks. Wet absorption technique utilizing a kjeldahl™ tubes were utilized for entire processing of washed fingernails [11].

Instrumentation

Chromium in nails was determined using JY 2000-2 ICP Optical Emission Spectrometer. The new JY 2000-2 will boost your laboratory's productivity with its high-performance and dependability at an affordable price. The

reasonably priced JY 2000-2 outperforms other radial ICP spectrometers that cost significantly more in terms of performance. The JY 2000-2 is the result of updating the tried-and-true design to include numerous cutting-edge ULTIMA 2 design elements. Typical 3 sigma detection limits for Cr=0.5 ppb.

Precision & Accuracy

accuracy and precision of (ICP-OES) instrument was affirmed by estimation of (Relative Standard deviation RSD%) and (%R) utilizing 10 reproduce estimations of "pooled" water test, and Standard reference material, all in all, great level of accuracy was acquired for most components with culminate estimation of 4.3% relative standard materials (Table 1). Estimated CRM esteems acquired for investigation of chromium via ICP-OES was exceptionally near to affirmed esteems. Logical recuperation esteem is 98.25% for chromium decided, as revealed in Table1. The detection Limits for chromium = 0.08 mg\kg.

Table1: Accuracy and precision level human fingernails samples (n = 20), respectively.

Accuracy(%R)				(Precision)
Element	Observation value SD	True value ± SD	Recovery %	RSD %
Cr(mg\kg)	**0 . 112 ± 0.009**	**0.114 ± 0.007**	**98.25**	**4.3**

Results and Discussion

Altogether, 122 human Fingernails tests were gathered from sound Iraqi people (n=55) and lung tumor patients (n=67) occupant in Karbala with a specific end goal of deciding the chromium levels of fingernails. This can be utilized to examine whether human fingernails can assume a critical part as a biomarker shown in Table 2.

Table2: Population data for chromium level (mg\kg) in fingernails.

Component	Variable	Con.(dry/weight, mg/kg)
Cr	Quartile of Lower	**0. 05**
	Average ± standard deviation	**0.17±0.03**
	% RSD	**100.44**
	Quartile of Upper	**0.26**
	Limit of Confidence p=0.05%	**0.03**
	Average +CI	**0.20**
	Average –CI	**0.14**

Effect of Lung Cancer

Convergence of basic follow components are homeostatic ally managed when the well-being status of people is under typical situations [12]. There is amassing proof that the digestion of a few follow components is modified in tumor, and may assume critical parts in the pathogenesis and advance of this ailment [13]. Numerous examinations have beforehand talked about the connection between follow components and growth for patients by contrasting them and sound people [14,15]. The after effects of sound people and lung disease patient inhabitant in Karbala have been contrasted all together to assess whether there is any huge contrasts in level of Cr between two gatherings {table 3}. This might be utilized to depict whether lung tumor assumes any huge part of these distinctions via expanding or diminishing chromium levels throughout the human body as a result of the impact on chromium digestion. Consequences of solid people and lung tumor patient occupant in Karbala have been contrasted all together with assess whether there are any critical contrasts in Cr level between 2 gatherings. This can be utilized to portray whether lung tumor assumes any critical part in these distinctions by expanding or diminishing Cr level within human body through impact on the digestion of basic components. Standard deviation and Mean value of Cr level in fingernails of lung malignancy populaces were thought about by utilizing a T-test & two-followed F-test, and the outcomes obtained are recorded in table3. In spite of the fact that level Cr is higher in lung disease patient (0.2757 ± 0.0209 mg/kg) than healthy (0. 0437 ± 0. 0044 mg/kg), however the distinctions are measurably important (P<0.05).The Mean values and SD of Cr in fingernail of lung cancer patient (0.2025±0.0117 mg/kg & healthy (0.0481±0.0045 mg/kg)as shown in table 4. It was found a level of Cr was higher in patient in comparison with healthy.

Table 3: Chromium standard deviation & Mean values for lung cancer patients and healthy individual**.**

	Mean values vales ± SD (mg/kg)		F-test			Two-tailed T-test			
	Healthy (n1 = 55)	Lung Cancer (n2 = 67)	Variance	*Fcalculate*	Signifcant	*t*calc	*df*	Signifcant	*t critical*
Cr	0.0437 ± 0.0044	0.2757 ± 0.0209	EVA UVA	20.36 -	0.000	9.893 5.425	120^{+} $71.^{++}$	> 001 > 001	**1.9890**

Table4: Chromium standard deviation & Mean values in human fingernail for lung cancer patients & healthy individuals (only non-smokers)

Cr	Mean values± SD (mg/kg)		F test			Two tailed t- test			
	Healthy (n =47)	patient (n = 32)	Variance	$F_{calculate}$	Signifcant	t_{calc}	*d.f.*	Signifcant	$t_{critical}$
	0.0481 ± 0.0045	0.2025± 0.0117	EVA UVA	24.54 -	< 0.001	13.88 12.28	77^{+} 40^{++}	0.059 0.223	**1.9890**

Influence of Gender

The aggregate populace from Karbala (n = 122) was partitioned into two sexual orientation gatherings, females and males. The impact of sexual orientation on level of Cr in fingernails tests was examined, and Mean values and standard deviation (±SD) of every sex gather are outlined {Table 5}. So as to decide if there are any huge distinction that can be credited to sex, a F-test & two-followed t-test were embraced on fingernails information from people. The discoveries demonstrate there is a noteworthy impact of sex on level of Cr ($t(120) = 5.246$, $t_{crit.values} = 1.9798$, $P_{values} = 0.05$), the quantity freedom degrees & basic esteem t_{crit} are resolved at likelihood levels at $P_{value} = 0.05$), consequences point toward more important amounted Cr in male ($0.\ 2230 \pm 0.0205\ mg/kg$) when compared with female ($0.0646 \pm 0.00987\ mg/kg$).

Table 5: Chromium standard deviation and mean values in human fingernails for male & female.

Cr	Mean values± SD (mg/kg)		F-test			2 tailed T-test			
	Males (N = 82)	Females (N = 40)	Variances	$F_{calculate}$	Significant.	Tcalculate	D.f.	Signifcant	t-*critical*
	0.2230 ± 0. 00202	0. 0646 ± 0. 00987	E.V.A U.V.A	12.846	0 .000	040.5 54956	002^{+} 002^{++}	>001 >000	**1.9798**

Influence of Smoking Activity

Smoking is one of the main causes of many diseases, including heart disease, atherosclerosis, lung cancer, and other diseases related to the respiratory system. [16,17]. Cigarette tobacco affects the immune system, as well as damage to the respiratory system and the general health of the individual [18]. Many studies have confirmed that cigarette tobacco has a negative impact on health, as well as the resulting pollutants on the environment. Previous studies have shown that cigarette tobacco contains many heavy metals that cause risks to human health. [19]. In our current study, samples of the nails of non-smokers were collected and compared with those of smokers to determine the percentage of chromium in both cases. The study found a higher level of chromium in smokers (0.2665 ± 0.0262 mg/kg) paralleled to non-smokers(0.0875 ±0.0103 mg/kg), and Table 6 shows this.

Table 6: Chromium standard deviation(SD) and Mean values in fingernail for non-smokers and smokers

	Mean values± SD (mg/kg)		F-test			2 tailed t-test			
	Smoker (N = 57)	Non smoker (N= 65)	Variance	$F_{\text{-calculate}}$	Significant	$t_{\text{-calculate}}$	*D.f.*	Significant	$t_{critical}$
Cr	0.2665 ±	0.0875±	EVA	13.59	0.000	6.647	120^{+}	< 0.001	**1.9798**
	0.0262	0.0103	UVA	-		6.347	73^{++}	< 0.001	

Influence of Age

Moreover, the impact of age was additionally considered to assess whether this parameter give any critical consequences for level of Cr in fingernails alongside different elements. The examination populace was isolated into 3 age gatherings: under twenty years old (n= 5), twenty–forty years (n= 22), & above 40 years (n= 95). SD. & Mean values at confidence limits = 95% certainty interim for Mean values of chromium levels in fingernail for samples {table 7}. One-way -ANOVA utilized for checking whether any critical contrasts were found between age gatherings of Cr level at Probability levels of P < 0.05. The outcomes demonstrate that there is a noteworthy contrast of chromium, as appeared in table 8. It were discovered there are a huge contrast (Pvalue under

0.05) some place between mean estimations chromium in fingernails for 3 gatherings {Table 8}. This does not give which amass is not quite the same as which different gatherings. In this way, the post-hoc test was utilized to decide if any huge contrasts between the gatherings, as appeared as shown in table 9.The outcomes demonstrate level of Cr in age gathering (more than multiyear) is altogether extraordinary when contrasted and the two outstanding gatherings (under 20 and 20 – multiyear) at the $P < 0.05$. Then again, there is no significant between the two cases (under 20 and 20 – multiyear), as appeared in table 9.

Table7: standard deviation & Mean values at 95% confidence limits for C

Age	n	Mean values ± SD (mg/kg)	CI at 95%	
			Lower.	Upper.
≤20	5	0. 0130± 0. 0115	0. 137	0. 163
20 – 40	22	0. 1293 ± 0. 2010	0. 058	0. 201
≥ 40	95	0. 1891 ±0. 1654	0. 155	0. 224

Table 8: Analysis of variance ANOVA for chromium level fingernail samples

Source of variance	Sum of Square	*D.f.*	Mean Square	*F.*	Significant.
Between--Group	1. 294	2	0.648	33.140	0 .000
Within-Group	2. 323	119	0.021		
Total	3.617	121			

Tab. 9 Post Hoc-test for chromium level using dissimilar age for samples

Age/ year		Mean values Variance (G1–G2)	SD. Errors	Sig.	CI (95%)	
G1	G2				Lower Bound	Upper Bound
≤20	20 to 40	0. 0360	0.04420	0.418	0.1236	0.0501
	Over40	0. 2432	0.04198	0.000	0.3264	0.1600
20 to 40	under20	0.0360	0.04420	0.418	0.0501	0.1236
	Over 40	0.2072	0.02279	0.000	0.2524	0.1621
Over 40	Under 20	0.3432	0.04198	0.000	0.1600	0.3264
	20 -40	0.2072	0.02279	0.000	0.1621	0.2524

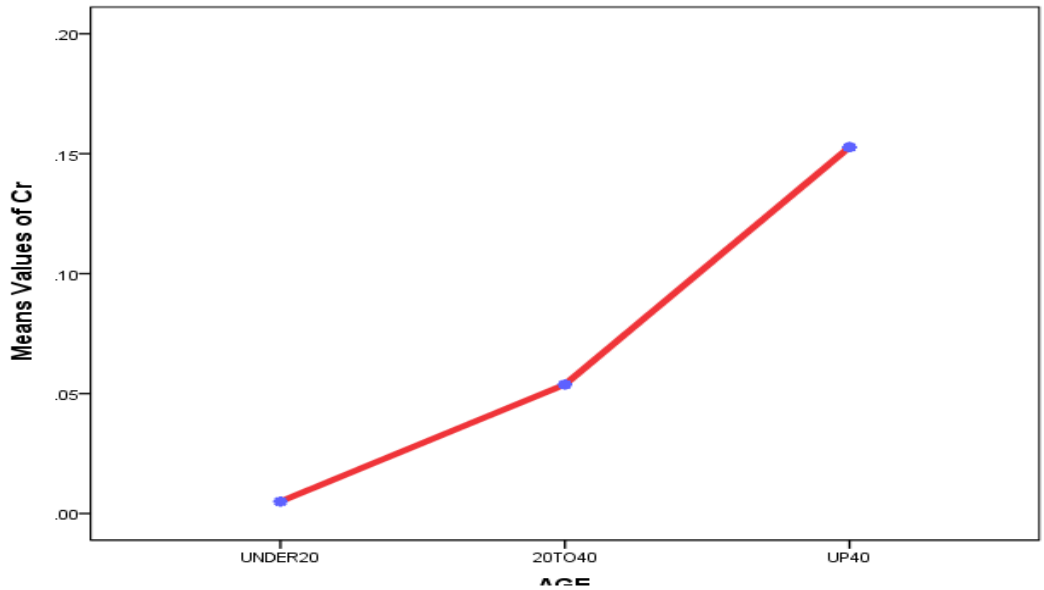

Figure 1: Con. of chromium in fingernail for under 20 year (n= 5), 20 - 40 year (n= 22) and above 40 year (n= 95) .

Conclusion

The inductively coupled plasma atomic emission (ICPAES) technique was applied to estimate trace concentrations of chromium in human nails of people with lung cancer. This technique was distinguished by its accuracy, efficiency, and high sensitivity to measure very trace concentrations of chromium. An elevated level of Cr in nail samples resulting from extended revelation to high level of Cr causes various diseases & disorders. Cr (VI) can use a variety of epigenetic pathways to change gene expression and induce the development of malignant tumors.

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