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## **Research Article**

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## Environmental Risk Factors and Plasma Concentration of Lead and Copper in Colorectal Cancer Patients in Alexandria

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Background: Colorectal cancer is the third most commonly diagnosed cancer in both men and women. It is thought to result from a complex interaction between several genetic factors and environmental factors. Recognizing these factors that trigger the disease occurrence and progression is essential to apply more effective measures of prevention and risk reduction. Objectives: The main objectives of this study were to detect the plasma levels of lead and copper in colorectal cancer patients and healthy subjects and to estimate the effect of exposure to some environmental risk factors. In addition, a booklet was designed for health education and prevention of colorectal cancer based on the results of the research. Methods: A case control study was performed at the clinical oncology department clinic of Alexandria Main University Hospital. The study sample consisted of 25 colorectal cancer patients, and 25 healthy controls, who matched the cases on age and sex. Data were collected by a pre-designed pre-coded structured interviewing questionnaire; levels of lead and copper of all participants were measured by graphite furnace atomic absorption spectrometry. In addition, lead and copper levels in the drinking water by participants were measured to detect whether they were associated with the risk of colorectal cancer. Results: Higher levels of Pb and Cu were detected in colorectal cancer patients compared to healthy subjects, these findings were statistically significant (p < 0.05). The multivariate stepwise logistic regression model revealed that four factors had significant association with colorectal cancer , the first rank was lead levels  $\geq 0.164$  mg/L, Passive smoking, living nearby the solid waste collecting dustbins and old oily wall paints in houses (OR =31.057, 95% CI =1.549-622. 588, OR =32.20, 95%CI =1.529-678.069, OR =83.247, 95%CI =1.279-5419.134, OR =9.354, 95%CI =1.020-85.786, respectively).Conclusion: According to the findings of this study, there was a significant difference in the levels of Pb and Cu levels between healthy subjects and colorectal cancer patients. Therefore, environmental risk factors and chronic exposure to lead sources such as lead in old deteriorating household paints could have a very important role in the elevated lead level due to the high rate of pollution in the environment. However, further studies are needed to enhance our understanding of this relationship between heavy metals and their role in cancer progression

## Keywords: Colorectal Cancer, Copper, Environmental Risk Factors, Lead.

## 1. Introduction

Colorectal cancer is considered as one of the most common digestive system malignancies that exhibits higher morbidity and mortality all over the world. Its prevalence rate is increasing largely in the recent decades especially in the developing countries. The etiology of colorectal cancer is not clearly understood, it is a multifactorial disease. Many factors could share in the pathogenesis of colorectal cancer such as genetic defects and environmental risk factors. About 5% to 10% of people who develop colorectal cancer have inherited gene defects that cause the disease. Many epidemiological studies have focused on the role of diet, environmental pollution, obesity, alcohol intake, social stress, tobacco smoking and high consumption of red meat (especially processed meat), low consumption of fruits, vegetables, dietary fibers, and sedentary life style as possible risk factors. Recently, many studies indicated the important role of environmental factors, including trace elements of heavy metals, these studies proved the strong association between the increased level of environmental pollution and colorectal cancer development assessed by the increased levels of different trace elements such as lead, cadmium, manganese and copper in patients with colorectal cancer compared to healthy controls. These factors could affect DNA and lead to genetic defects by generation of reactive oxidative species (ROS) which causes ineffective DNA repair and leading to carcinogenesis. This gives an alarm for the importance of increasing the public health awareness about environmental risk factors (1). Emre et al., had proved the previously mentioned relationship (2). Another case control study was conducted by Sohrabi et al., had proved the increased levels of heavy metals in the cancerous tissue of colorectal cancer patients compared to the normal neighboring tissue in the same patients and it was statistically significant, (p < 0.05) (3). So, the present study aimed to measure the level of lead and copper in colorectal cancer patients and healthy controls and to measure the level of lead and copper in drinking water samples consumed by cases and healthy controls. It aimed also to identify environmental risk factors of colorectal cancer then to determine the relation between identified environmental risk factors and level of lead and copper in colorectal cancer patients.

## 2. Methodology

The present study started in November 2019 and until reaching the required sample size in April 2020. It was followed by data entry and data analysis that took about 6 months ending in October 2020, a total of twenty five patients with colorectal cancer and twenty five healthy individuals matched to cases on age and sex were enrolled. Venous blood samples of all participants in accordance with the guidelines set out in the Declaration of Helsinki. In- formed consent was given by all the patients included in this study. The study was approved by the local ethics committee. Serum was separated by centrifugation and the samples were processed immediately. The serum samples were placed in deionised polyethylene tubes and kept at -80°C (without thawing) until samples were analyzed. Determination of serum concentrations of lead and copper by flame atomic absorption spectrometry after wet digestion of the plasma samples. Appropriate statistical procedures were then applied to process the data using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and

percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level. A results was considered statistically significant when the significance probability was less than 5 % (p< 0.05) .A structured interviewing predesigned questionnaire was administered to participants and was used to collect data from cases and controls. Data included: personal and socio-demographic data, medical history, lifestyle, dietary habits, indoor and outdoor environmental exposures.

## 3. Results

The study sample consisted of 25 cases of colorectal cancer that were confirmed by the consultant before starting chemotherapy or surgery and 25 healthy subjects, cases had an age range of (23-67)years, while the control group had an age range of (25-64)years. There is no difference was detected between the two groups because they were matched on age and sex, 52% of each group were males and 48% were females. The socio-demographic characteristics of the studied sample (presence of family history, family number, occupation, educational level, comorbid diseases and use of medications), it was noted that about 16% of cases were less than 40 years old.

## 4. Discussion

Table (1) showed that high household crowding index (2+) was detected in (56%) of the cases compared to (16%) of controls. Cases had 6.68 times more risk to develop colorectal cancer compared to controls (OR=6.682; 95% CI: 1.1769 – 25.245). It was noted that about (80%) of cases were having lower income compared to (20%) of controls that had an impact on the increased risk of cases to develop colorectal cancer 16 times more than controls (OR=16.0; 95% CI: 4.0 - 63.975). By assessing the association between level of education and colorectal cancer, there was a significant difference between cases and controls, the cases with low education (illiterate) were 9.5 more risk to develop colorectal cancer than controls (OR=9.5; 95% CI: 1.579 -57.16). On the other side, the cases with secondary /above intermediate education had 5.4 more risk to develop colorectal cancer compared to controls (OR=5.4; 95% CI: 1.059 - 27.833),that proved the beneficial effect of education as protective factor in colorectal cancer. These results were consistent with the study done in 2010 to detect the impact of educational level on the incidence rate of colorectal cancer in women and significant association was detected that education is a protective factor(p<0.05), and the incidence rate was higher in women with lower educational level(4). This result was supported by another recent cross sectional study among colorectal cancer patients conducted in Ethiopia, it reported that the high level of education and females had better awareness about colorectal cancer, it was statically significant (P<0.05) (5).

This finding was in accordance with a retrospective cohort of 18,492 Patients with colon cancer that reported a high mortality rate of patients lived in communities with the lowest

socioeconomic level had compared with others who lived in communities with the highest socioeconomic status (hazards ratio (HR), 1.19; 95% confidence interval (95% CI), 1.13– 1.26; P < .001) (6). Another study supported the same idea and reported that the low SES patient of colorectal cancer had poor survival, poor prognosis and were admitted to health care facilities in late stages (7).

Concerning the presence of comorbid diseases, it was found that cases with comorbidities(diabetes, hypertension and irritable bowel diseases) were 4.75 times more risk to develop colorectal cancer than those who do not (OR=4.75; 95% CI: 1.406 - 16.051). The risk of developing colorectal cancer was higher in cases using medications 4 times more than controls (OR=4.33; 95% CI: 1.235 - 15.21). It was noted that 32% of the cases were diabetic and hypertensive compared to only 20% of controls.

Table (2) presented the association between environmental tobacco smoke (ETS) and colorectal cancer, it was found that cases who were exposed to Environmental tobacco smoke (ETS) had about 8 times more risk to develop colorectal cancer than controls (OR=7.944; 95% CI: 1.884 – 33.498) .This result was consistent with a cross sectional study was conducted to estimate the association between ETS and colorectal cancer risk, exposure to ETS was found to be associated with colorectal cancer in all subjects (fully adjusted odds ratio (OR), 1.95; 95% confidence interval (CI), 1.08-2.44; P = 0.001) (8). This result was in the same line with a study conducted by Samowitz et al. (9). It reported that smoking was associated with an approximately twofold increased risk of the CpG island methylator phenotype (CIMP) high colon cancer with mutant BRAF and microsatellite stability (for those smoking >20 cigarettes per day, (OR = 1.92, 95% CI = 0.67 to 5.51), so cigarette smoking was associated with an increased risk of colon cancers. Cases who used insecticides with high rate had 5.46 times more risk to develop colorectal cancer than those who don't use insecticides of control group (OR=5.46; 95% CI: 1.627-18. 352). An epidemiological study conducted by Soliman et al., (10) that revealed an increased serum level of organochlorine pesticides in Egyptian patients with colorectal cancer. Another study supported the idea that pesticides are a risk factor for solid tumors (11).Drinking water considered being one of the main sources of trace heavy metals. It was detected that (72%) of cases who had drinking water problems (changing the color or odor, turbid water, and inadequate water source) had 13.5 times more risk to develop colorectal cancer compared to controls (p < 0.05), (OR=13.5; 95% CI: 3.395 – 53.682).Concerning the type of water pipes in houses of cases, it was found in(56%) had old water pipes in their houses compared to only (8%) of controls(p<0.01), and they had 14.6 more risk to develop colorectal cancer than those with new plastic water pipes, (OR=14.6; 95% CI: 2.82 - 75.954)...Regarding the assessment of waste water problems, it was detected that (36%) of cases had problems in waste water in the areas of their residence compared to (8%) of controls (p<0.01), with 13.5 times more risk to develop colorectal cancer than those who do not of the control group,

(OR=13.5; 95% CI: 1.556 – 117.137). When asking about the fuel source used in houses, it was detected that (52%) of cases were using butane as a fuel source compared to (8%) of controls, (p<0.05) and they had 12 times more risk to develop colorectal cancer than those who use natural gas (OR=12; 95% CI: 23.407 – 64.495).

Table (3) showed that cases who worked >7 hrs. /day had 33 more risk to develop colorectal cancer than control group (OR=33; 95% CI: 4.74 - 229.65). This could be explained by excess exposure to harmful risk factors in work place for long time. Regarding the assessment of harmful effect of chronic exposure to outdoor environmental risk factors especially air pollution caused by industrial exhausts, firing garbage and accumulation of solid waste in many residential areas ,it was noted that the risk of colorectal cancer development in cases lived nearby mobile phone stations, cases were 9 times of higher risk than controls (OR=9.33; 95% CI: 1.052 - 82.780), and it was detected that cases lived nearby waste dustbins were 4 times more risk to develop colorectal cancer than controls,(OR=4.125; 95% CI: 0.961 - 17.04) and it was estimated that the cases lived nearby area of firing Garbage had 11 times more risk to develop colorectal cancer than controls, (OR=11.294; 95%) CI: 1.29 - 98.889). Concerning the dietary habits, it was found that cases with excess consumption of carbonated beverages (64%) compared to (28%) of controls p=0.01 had 4.57 times more risk to develop colorectal cancer, (OR=4.57; 95% CI: 1.383 - 15.109). It was estimated that cases with exposure history to noise and excess vibrations had 39 times more risk to develop colorectal cancer than controls. Also it was noted that about 48% of cases were working as drivers and in industry compared to 12% of controls (p<0.01), this may explain the impact of air pollution on health after long exposure time (OR=39; 95% CI: 4. 022 - 378.199). ). This finding could be assessed by a retrospective study conducted in China, 2000 among colon cancer cases diagnosed between 1980 and 1984 in Shanghai, and they were classified by job types and physical activity levels. Men employed in occupations with low physical activity levels had modest but significantly increased risks of colon cancer. Increased incidence was observed for professional and other white collar workers, and male chemical processors and female textile workers. The findings add to the emerging evidence that workplace activity may enhance the risk for colorectal cancer (12). Cases who were exposed to chemical risk factors had 11 times more risk to develop colorectal cancer than controls (OR=11; 95% CI: 2.157 – 56.094). In an epidemiologic study conducted to detect the relation between increased risk of colorectal cancer and workplace exposures, it found that the high exposure to dyes, solvents, and grinding wheel dust in workplace increased the risk for colorectal cancer (13). This result was consistent with another study performed by Gwini et al., on workers exposed to inorganic lead revealed that lead levels were significantly higher in colon cancer patients when compared with healthy group (14).

In table (4), it was noted that mean concentration of heparin plasma Pb level in cases was  $(0.45\pm0.048)$ mg/L, and it is double the value of mean concentration of Pb in controls

(0.21±0.25)mg/L, about 64% of the cases with lead level (> 0.164 mg/L), had about 4 times more risk to develop colorectal cancer compared to 32% of controls with lead level less than (0.164 mg/L (OR=3.778; 95% CI: 1.170 - 12.194). It was detected that 56% of the cases with copper level (>1.3 mg/L) had high copper% had 3 times more risk to develop colorectal cancer compared to 28% of controls with copper level less than(1.3 mg/L) (OR=3.273; 95% CI: 1.008 -10.621). There was a significant positive correlation between the levels of lead and copper in cases. It was noted that 72% of the cases had high lead level in drinking water (> 0.061mg/L) had 10 times more risk to develop colorectal cancer compared to 20% of controls with water lead less than( 0.061 mg/L)(OR=10.286; 95% CI: 2.67- 38.215). It was noted that 17% of the cases had high copper in drinking water (> 0.012mg/L) had 11 times more risk to develop colorectal cancer compared to 4% of controls with water copper less than (0.012mg/L) (OR=10.286; 95% CI: 2.864 – 43.464).By performing a multivariate stepwise logistic regression analysis, four factors showed significant association with colorectal cancer. Lead level (Pb) level (>0.164) mg /L, passive smoking, living nearby waste dustbins and the type of wall covering paints (old oily paints) (OR= 31.057 (95% CI: 1.549 -622.588), OR= 32.2(95% CI: 0.625-52.024, OR= 9.354 (95% CI: 1.02-85.786), OR=83 (95%CI: 1.279-5419. Respectively) as presented in table (5). Area under a curve (AUC) for ROC curve of lead was (0.686) and the optimal cut-off point to diagnose colorectal cancer was (> 0.164) mg/L Table (4.13). The cut-off point of (> 0.164) revealed high sensitivity (64%) and high specificity (68%) as presented in table (5). The ROC curve was plotted for colorectal cancer patients by using their lead level cutoff points as shown in figure (1) After categorization of lead level in the sample, the odds ratio was calculated for high level groups compared to the reference group (<0.164 mg/L). Cases with lead level (> 0.164) mg/L were 3.7 times more risk to develop colorectal cancer compared to whom lead level (< 0.164), (OR=3.778; 95% CI: 1.170 – 12.194). The mean concentration of lead level in cases was  $(0.45 \pm 0.48)$  mg/L and it was significantly higher than the control group  $(0.21 \pm 0.48)$ 0.25) mg/L as U=196.50<sup>\*</sup>, p=0.024, the mean lead level of the case group was twice the mean of control group. Only 32 % of control group compared to 64% of case group had high lead level (> 0.164) in respect to the risk of colorectal cancer. There was a significant difference ( $\chi^2 = 5.128$ , p=0.024).

#### Conclusion

It was evident from the results that colorectal cancer is multi-factorial disease, where many risk factors interact and contribute to its development. The current study showed that the environmental exposures and the possible etiological mechanisms in colorectal cancer development would allow us to reduce the incidence and prevalence rates and better health care policies would be adapted to improve early detection of the disease. Also it would be reflected on the economic side presented in saving economic resources and opportunities for patients, families, employers and society and avert the substantial burden of the disease.

#### Summary

The present study could be considered a good starting point towards more interest and efforts to be done to reduce the highly increased environmental pollution nowadays.

Enhance the public health awareness about the harmful effect of chronic exposure to

environmental pollutants on human health and to give a good reason for more behavioral changes in life.

Regarding the effectiveness of health education in the improvement of public awareness and screening rate of colorectal cancer. And after reviewing of literature and analyzing the results of the present study, the booklet was designed to enhance the public awareness about colorectal cancer.

A booklet is a small book with fewer pages and smaller dimensions than a "real" book. Data were collected from the literature review and from the results of the study to design the booklet.

The booklet was written with clear readable fonts, and designed in a simple Arabic language with colored figures to help illiterate personal to profit from recommendations and advices included.

The booklet is aiming at enhancing the public health awareness about the environmental risk factors related to colorectal cancer.

Colorectal cancer prevention at different levels; behavioral modification, early detection (screening) and improve the life quality.

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Controls® Cases Test of Socio-demographic (n = 25)(n = 25)р OR (95% CI.) characters Sig. % No. % No. Educational level Illiterate • 0.015 9.5(1.579-57.16) 28.0 2 8.0 7  $\chi^2 =$ Primary 0.018  $11.62^{*}$ 20.0 1 4.0 13.57(1.39-137.45) 5 Secondary 0.05 6 24.0 3 12.0 5.429(1.059-27.833) Higher education® 7 28.0 19 76.0 1.000 Family income 20 80.0 5 20.0 16.0(4.0-63.975)  $\chi^2 =$ 0.001 Not enough  $18.00^{*}$ 5 20.0 80.0 20 1.000 Enough® **Crowding index**  $\chi^2 =$ 1-® 11 44.0 21 84.0 0.003\* 1.000 8.681\* 14 56.0 4 16.0 6.682 (1.769–25.245) 2+**Comorbidities**  $\chi 2 =$ 15 60.0 6 24.0  $0.010^{*}$ 4.75 (1.406 - 16.051) Yes 6.650\* 10 40.0 19 76.0 1.000 No® Use of medications  $\chi^2 =$ 20.0 13 60.0 5 Yes 0.018 4.333 (1.235 – 15.21)  $5.556^{*}$ 12 40.0 80.0 20 1.000 No®

 Table (1): Estimation of the risk of colorectal cancer in relation to some socio-demographic factors (Alexandria Main University Hospital, 2020).

 $\chi^2$ : Chi square test, OR: Od

OR: Odds ratio,

®: Reference group

CI: Confidence interval, P: p value for comparing between the studied groups

Table (2):Estimation of the risk of colorectal cancer in relation to indoorenvironmental risk factors (Alexandria Main University Hospital, 2020)

	Cases		Controls®												
Indoor environmental risk factors	(n = 25)	(n = 25)		5)	Test of Sig.	Р	OR (95% CI.)								
	No.	%	No.	%	~-8										
Exposure to ETS					_										
• Yes	13	52.0	2	8.0	$\chi^2 = 9.191^*$	0.002	7.944 (1.884 – 33.498)								
• No®	12	48.0	23	92.0			1.000								
Water problems															
• yes	18	72.0	4	16.0	χ <sup>2</sup> =	0.001*	13.5(3.395–53.682)								
• No®	7	28.0	21	84.0	$\chi^2 =$ 13.235 <sup>*</sup>	0.001	1.000								
Water pipes	14	56.0	2	8.0	2		14.636 (2.82 – 75.954)								
• Old pipes	11	44.0	23	92.0	$\chi^2 = 16.095^*$	<0.001*	1.000								
• Plastic pipes®															
Waste water problems															
• Yes	9	36.0	1	4.0	$\chi^2 = 8.00^*$	<0.011 <sup>*</sup>	13.5 (1.556 – 117.137)								
• No®	16	64.0	24	96.0			1.000								
Fuel source															
• Butane	13	52.0	2	8.0	$\chi^2 = 11.524^*$	$0.001^{*}$	12.458 (2.407 – 64.49)								
Natural gas®	12	48.0	23	92.0			1.000								
Wall covering paint															
• Old oily paint	20	80.0	6	24.0	$\chi 2 =$	<0.001*	12.667 (3.308 - 48.504)								
• New paint®	5	20.0	19	76.0	15.7*		1.000								
Use of insecticides															
• sometimes	18	72.0	8	32.0	χ <sup>2</sup> =	0.007	5.464 (1.627 – 18.357)								
• No®	7	28.0	17	68.0	8.013 <sup>*</sup>	0.005	1.000								
$\chi^2$ : Chi square test, OR:	Odds ra	tio,	R:	Referen	ce group	$\chi^2$ : Chi square test, OR: Odds ratio, (B): Reference group									

CI: Confidence interval, p: p value for comparing between the studied groups \*: Statistically significant at  $p \le 0.05$ 

Place of residence	Cas	es	Cont	Controls®					
	(n =	· · ·	(n =	-	Test of Sig.	р	OR (95% CI.)		
Nearby:	No.	%	No.	%	515.				
Mobile phone station									
• Yes	7	28.0	1	4.0	. 2	FE	0 222 (1 052 02 790)		
• No ®	18	72.0	24	96.0	$\chi^2 = 5.357^*$	<sup>FE</sup> p= 0.045 <sup>*</sup>	9.333 (1.052 –82.780) 1.000		
Waste dustbins									
• Yes	9	36.0	3	12.0	$\chi^2 = 3.947^*$	0.043*	4.125 (0.961 – 17.704)		
• No®	16	64.0	22	88.0	5.947		1.000		
Firing garbage						FF			
• Yes	8	32.0	1	4.0	$\chi^2 = 6.640^*$	<sup>FE</sup> p= 0.023 <sup>*</sup>	11 20 4 (1 20 00 000)		
• Tes • No®	17	68.0	24	4.0 96.0	6.640*	0.023	11.294 (1.29 – 98.889) 1.000		
Working									
hrs./day	11	70 (	2	10.0	$\chi^2 =$	0.001	22.00(4.742.220.)		
• >7hrs	11	78.6	2	10.0	$\chi^2 =$ 16.397	0.001	33.00(4.742–229.)		
• <=7hrs ®	3	21.4	18	90.0			1.000		
Socio-									
environmental									
Risk factors					$\chi^2 =$	0.000			
• Yes	12	85.7	8	40.0	$\chi^2 = 7.105^*$	0.008	9.00(1.574–51.47)		
• No®	2	14.3	12	60.0			1.000		
Physical risk factors					2				
• Yes	13	93.0	5	25.0	$\chi^{-}=$	< 0.001*	39 (4.02 –378.19)		
• No ®	1	7.0	15	75.0	10.221		1.00		
Chemical risk factors					$\gamma^2 =$				
• Yes	11	78.6	5	25.0	$\chi^2 = 9.487^*$	0.002	11 (2.157–56.094		
• No ®	3	21.4	15	75.0			1.000		

Table (3): Estimation of the risk of colorectal cancer in relation to place of residence and some factors at the work place (Alexandria Main University Hospital, 2020).

FE: Fisher Exact, OR: Odds ratio,

®: Reference group

 $\chi^2$ : **Chi square test,** CI: Confidence interval,

p: p value for comparing between the studied groups \*: Statistically significant at  $p \le 0.05$ 

Table (4):	Estimation of the risk of colorectal cancer in relation to lead and copper
	plasma levels (Alexandria Main University Hospital, 2020).

	Cases (n = 25)		Controls <sup>®</sup> (n = 25)		Test of	Р	OR (95% CI.)	
	No.	%	No.	%	Sig.			
Pb level								
(mg/L)								
(≤0.164) <sup>®</sup>	9	36.0	17	68.0	$\chi^2 = 5.128^*$	0.024*	1.000	
(>0.164)	16	64.0	8	32.0	5.128*	0.024	3.778 (1.170 – 12.194)	
Min. – Max.	0.04 -	- 1.76	0.003 - 0.94					
Mean ± SD.	0.45 =	± 0.48	$0.21 \pm 0.25$		U= 196.50 <sup>*</sup>	$0.024^{*}$	_	
Median (IQR)	0.21 (0.1	1 – 0.66)	0.13 (0.05 - 0.30)		190.50			
Cu level (mg/L)								
$(\leq 1.3)^{\mathbb{R}}$	11	44.0	18	72.0	$\chi^2 = 4.023^*$	$0.045^{*}$	1.000	
(>1.3)	14	56.0	7	28.0	4.023*	0.045	3.273 (1.008 - 10.621)	
Min. – Max.	0.79 -	- 3.79	0.10 - 1.84					
Mean ± SD.	1.46 -	±0.64	$1.10 \pm 0.41$		U= 206.50 <sup>*</sup>	$0.040^{*}$	_	
Median (IQR)	1.36 (1.0	5-1.61)	1.08 (0.	88-1.31)				

 $\chi^2$ : **Chi square test,** CI: Confidence interval, U: Mann Whitney test, OR: Odds ratio, ®: Reference group

p: p value for comparing between the studied groups \*: Statistically significant at  $p \le 0.05$ BEI (Biological Exposure Index of Pb in plasma=0.0001mg/L) = (1.00 µg/L) in adults

<b>Table (5):</b>	Area under the ROC curve of lead levels (Alexandria Main University	r
	Hospital, 2020).	

	AUC	Р	95% CI	Cut off	Sensitivity	Specificity	Δ	NPV
Pb level (mg/L)	0.686	0.024*	0.539 - 0.832	>0.164#	64.0	68.0	66.7	65.4

AUC: Area Under a Curve pCI: Confidence Intervals NPV: Negative predictive value \*: Statistically significant at  $p \le 0.05$ 

p value: Probability value

PPV: Positive predictive value

<b>Table (6):</b>	Analysis of risk factors affecting the risk of colorectal cancer by logistic
	regression (Alexandria Main University Hospital, 2020).

In donon don't voriables	D		<b>O</b> D	95% CI		
Independent variables	В	p-value	OR	LL	UL	
Pb level (mg/L) (>0.14)	3.436	$0.025^{*}$	31.057	1.549	622.588	
Cu level (mg/L) (>1.3)	1.741	0.123	5.703	0.625	52.024	
ETS Exposure	3.472	0.026*	32.20	1.529	678.069	
Cell phone stations	0.575	0.709	1.778	0.087	36.390	
Carbonated beverages Consumption	1.916	0.117	6.791	0.621	74.290	
Old oily wall paints	2.236	0.043*	9.354	1.020	85.786	
Living nearby Waste dustbins	4.422	0.038*	83.247	1.279	5419.134	
Constant	-6.560	0.004*				

B: Unstandardized Coefficients

CI: Confidence interval

OR: Odds ratio

\*: Statistically significant at  $p \le 0.05$ 

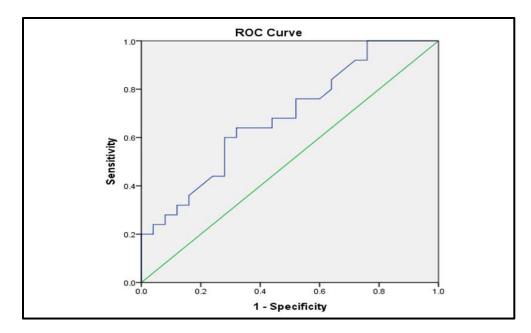


Figure (1): ROC curve of lead levels (Alexandria Main University Hospital, 2020

## Declarations

## Ethics approval and consent to participate

All authors agree and approve the article for publication

## **Consent for publication**

I hereby declare that no part of this article has been submitted to any other journal for publication

## Availability of data and materials

All data and materials are available up on request.

## **Competing interest**

No conflict of interest

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## Author's contributions

**Dr. Soha Said Mohamed** is the principle researcher, she carried out the practical part and wrote the manuscript with the help of the other authers. **Prof dr. Mamdouh hanafey abdou** helped in the selection and development of the research objectives. **Dr. Mohamed fakhry** and **Prof dr. Mohamed farouk** helped in the review of data analysis and guiding the work till the final step

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