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ANTIOXIDANTS, BIOCHEMICAL, AND HEMATOLOGICAL PARAMETERS CHANGE IN WORKERS OCCUPATIONALLY EXPOSED TO RADON INHALATION AT CERTAIN CONSTRUCTION MATERIAL INDUSTRIES IN ERBIL, IRAQ

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ABSTRACT:

This study examined the effects of radon on the endogenous antioxidants, biochemical, and hematological parameters of workers in Erbil, Iraqi Kurdistan. This was carried out to ascertain how radon affects the health of those who work in certain factories producing building materials. The case study group consisted of 70 workers, who were then divided into seven subgroups (gypsum, cement plant, lightweight block, marble, red brick 1, crushed stone, and concrete block 2), while the control group consisted of 20 healthy volunteers. The total antioxidant capacity (TAC), levels of carcinoembryonic antigen (CEA), superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX), the complete blood count (CBC), and liver function tests were evaluated. The statistical analysis revealed that the antioxidant activities and CEA levels between the case study group and the control group differed significantly. Also, antioxidant enzyme activities and indoor radon concentration, the annual effective dosage, were found to be highly significantly correlated by Pearson and Spearman analyses in the case study group. Additionally, the results demonstrated a substantial correlation in the data between the levels of CEA biomarkers and radon ($r=0.478$, $p<0.000$). The present results showed that radon concentration increased alanine aminotransferase (ALT) activity in a radon concentration-dependent manner ($r=0.263$ and $p<0.05$). The aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin activities, on the other hand, were not significantly affected by radon. The most significantly influenced CBC parameter was the low white blood cells (WBC) in the case study group compared to the controls. Low platelet count (PLT) was the second-highest problematic metric. The other CBC values, however, did not significantly differ between the research group and the control group. This study offers a preliminary image of the endogenous antioxidant systems in employees, especially to show a connection between radon and the occurrence of cancer among workers in Iraq Kurdistan Region.

KEYWORDS: Antioxidants; Blood; Hematology; Liver Function; Oxidative Stress; Radon

1. INTRODUCTION

The radioactive decay of uranium naturally produces the colorless, odorless gas known as radon. Radon is a gas that naturally occurs in the atmosphere, though it is present in very small amounts. It can also leak through building materials, rocks, soil, and groundwater. Radon decays to daughters with an alpha particle emission rate of 3.82 days (Ramadhani et al., 2021, Othman et al., 2022, Autsavapromporn et al., 2018, Grzywa-Celińska et al., 2020). It has been demonstrated that the radiolysis of water, an indirect radiation impact, causes the rapid production of reactive oxygen species (ROS) when eukaryotic cells are exposed to ionizing radiation. Rapidly rising ROS damages of cellular biomolecules such as lipids, proteins, and DNA are due to oxidative stress (Ahmad et al., 2016, Spitz et al., 2004). The consequences of radiation on the liver, and blood vessels result in hematopoietic syndrome. After exposure, symptoms like anorexia, lethargy, nausea, and vomiting may start to appear. The bone marrow, spleen, and lymph nodes begin to waste and do not usually replace the blood- forming cells once such symptoms have subsided. Hence, a deficiency in platelets and red blood cells occurs after a deficiency in white blood cells.

Moreover, an insufficient supply of platelets may cause hemorrhaging from organs, and sicknesses can result from a deficiency of white blood cells (Akleyev et al., 2010, Shahid et al., 2015).

It is well known that alpha particles emitted from radon decay products have a high linear energy transfer but a low penetrating power. Reactive oxygen species (ROS) such as hydrogen peroxide H_2O_2, singlet oxygen $^1O_2$, superoxide anion $O^{2.-}$, and hydroxyl radicals $OH^{\cdot}$ have been produced due to exposure to alpha particles (Ramadhani et al., 2021, Yanxiao et al., 2019, Kuciel-Lewandowska et al., 2018b, Ahmad et al., 2016). Excessive ROS and oxidative stress lead to necrotic and apoptotic cell death, which harms cells and tissues. The liver is the main ROS target. Oxidative stress damages liver parenchymal cells, the major functioning cells (Li et al., 2015). ALT, AST, and ALP values indicate liver disease. Based on projections, ionizing radiation causes organ damage through oxidative stress. When the liver is damaged by cirrhosis or hepatitis, these enzymes rise rapidly (Abdelhalim and Moussa, 2013). Organisms that live depend on several antioxidant

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pathways to regulate the ROS created locally (by the mitochondrial electron transport system, for example) and externally due to reactivity with the surrounding area (such as ionizing radiation) and defend against oxidative damage to the cell. Humans have both endogenous and exogenous antioxidant defenses, which come from dietary sources such as dietary supplements, carotenoids, and polyphenols. Enzymes and small chemicals generated by cells called endogenous antioxidants work in tandem to control ROS levels. The most important non-enzymatic antioxidant is tripeptide glutathione (GSH), while antioxidants produced by enzymes comprise SOD, CAT, and GPX (Ahmad et al., 2016, Kuciel-Lewandowska et al., 2018b, Ramadhani et al., 2021). SOD catalyzes the transformation of $O^{2.-}$ to H_2O_2, which subsequently breaks down into oxygen and water by catalase and/or GPX (Kono and Fridovich, 1982, Ahmad et al., 2016).

GSH is necessary for GPX to reduce hydroperoxides. Additionally, it is well acknowledged that GSH functions as the main tiny cellular molecules reducing agent to shield cells from oxidative damage (Shimizu et al., 1998). There is stability between ROS generation and antioxidant capability in healthy subjects. However, a phase of illness or persistent radiation exposure can disrupt this equilibrium and cause oxidative stress (Chakraborty et al., 2009, Ahmad et al., 2016). According to earlier investigations (Đurović et al., 2008, Akköse et al., 2003, Venneri et al., 2009), the blood lipid peroxidation and antioxidant state of radiography professionals exposed to ionizing radiation may have changed. Radon has been identified as a human carcinogen. Analyses of data on underground miners repeatedly exposed to radon progeny provide a significant portion of our information regarding the carcinogenic consequences of radon. Although the precise chemical pathways underpinning radon poisoning are yet unknown, radon is the second most common factor in lung cancer (LC) (Walczak et al., 2019, Stanley et al., 2019). A link between radon exposure and an uptick in lung cancer incidence among uranium miners exposed to high radon concentrations has also been found (IARC, 2001).

Lung cancer assessment and surveillance often use serum tumor markers, with carcinoembryonic antigen (CEA) being one of the most responsive (Moertel et al., 1993). CEA, a glycoprotein involved in cell adhesion, is generated during prenatal development and released before birth. CEA is a cell-surface glycosylphosphatidylinositol (GPI) glycoprotein. It is an L- and E-selectin ligand. Healthy adults rarely have it in their bloodstream (Thomas et al., 2008). Colorectal cancer biomarker (CEA) is widely accepted. However, it also plays important roles in lung cancer diagnosis, progression, recurrence, metastasis, and treatment outcomes (Kozu et al., 2013). According to research, radon exposure causes lung cancer to develop over time (Collier et al., 1999, Gilbert et al., 1996, Nie et al., 2012). Residents irradiated with plenty of interior radon concentrations showed altered SOD and GPX activity, according to a previous study(Ramadhani et al., 2021). Even though there was a highly noteworthy ($p<.001$) confident connection between SOD and GPX activity (Ramadhani et al., 2021). According to previous researches, the relative lifetime risk of lung cancer is increased by 16% for every 100 Bq/m^3 of chronic radon exposure (Darby et al., 2005, Krewski et al., 2006).

According to our knowledge, few investigations have examined changes in the quantities of antioxidants in workers exposed to radon acutely at high levels or chronically at intermediate concentrations. Additionally, the scant studies that did so measured antioxidant levels using plasma or serum samples. The precise ROS that causes oxidative stress in workers exposed to ionizing radiation over an extended period is still unidentified, and it is also unclear how these outcomes vary depending on the type of occupational situation in building material factories. In this work, we sought to determine changes in endogenous antioxidant levels related to exposure to indoor radon levels among workers in different construction material industries in Erbil city. To achieve this, we assessed the levels of SOD, catalase, and GPX, three important antioxidant enzymes, and TAC. There isn't yet a serum biomarker that can be used to find out if someone is at high risk for lung cancer (LC) in places with high radon levels, but it is important to look into possible blood tumor markers that can confirm the diagnosis of LC caused by too much radon exposure. We looked at the levels of CEA in the blood of workers who were exposed to radon as a tumor marker for LC. We compared these levels to levels found in the blood of university staff as a control group.

2. MATERIALS AND METHODS

2.1. The study area

This research was conducted in the area of several specific construction material factories in Erbil City (the capital of Kurdistan Region) between latitudes 35 and 36 North and 43 and 44 East. Erbil has a total area of 80,000 km^2 and an estimated resident of more than two million. The positions of the specimens on the map were established, as indicated in Figure 1.

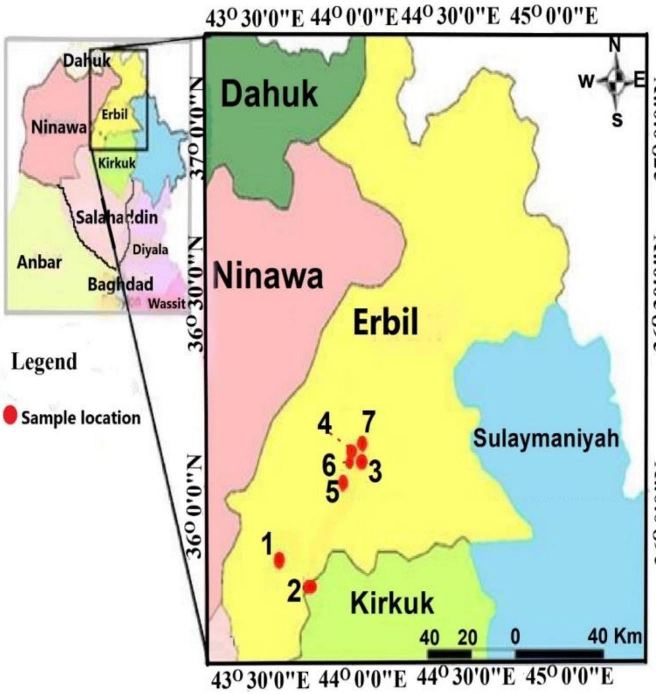

Figure 1: The samples' location under the study area (Othman et al., 2023)

2.2. Ethical approval

According to the guidelines of the Helsinki Declaration, this study was conducted. The University of Salaheddin's Ethics Committee approved it (13/06/2022/4s/89).

2.3. Radon concentration

Based on the findings of our earlier research, indoor radon concentrations and the annual effective dosage were assessed in a selection of material factories used in the construction of structures in the city of Erbil (Othman et al., 2022). The levels of radon were in a range of 21 to 190 Bq.m^{-3}, with an average value of 86.3 ± 6.9 Bq.m^{-3}. The average yearly lung cancer rate per 10^6 persons was determined to be (94.125), and the average value of the annual effective dose was equal to 2.179±1 mSv.y^{-1} (Othman et al., 2022), below and within the range of the reference level of (3–10) mSv.y-1 of the ICRP recommendation. Table 1 shows the demographic information, representative worker codes, radon concentration, and annual effective dose within the selected factories.

Table1: Case under investigation

Case group		**Sample code for workers**	**Radon concentration inside factories (Bq.m^{-3})**	**Annual effective dose (mSv.y^{-1})**
Factory No.	**Type of Factory**			
1	Gypsum	1-10	26.72	0.67
2	Cement plant	11-20	127.37	3.21
3	Lightweight block	21-30	107.81	2.72
4	Marble	31-40	113.44	2.86
5	Red brick 1	41-50	177.44	4.48
6	Crusher stone	51-60	87.5	2.21
7	Concrete block 2	61-70	54.46	1.37
Control group		71-90		

2.4. Blood sample collection

In this experiment, a total of 70 healthy workers as a study group (classified into seven subgroups of 10 workers) and 20 University staff as a control group have been taken. The ethical and regulatory issues related to the participants blood samples used in this experiment was approved by Salahaddin University's ethics committee of College of Science in the reference number (13/06/2022/4s/89) and was in accordance with the Declaration of Helsinki. Written informed consent was attained from all the participants. The age range for the case study group included in this study was 25–68 years, with an average value of 42.3±10.20 years. The age of the control group was 43.3±12.00 (mean ±SD; range: 25–65 years) (Othman et al., 2023). All workers were asked a thorough questionnaire about their habits, lifestyles, medical histories, age, abstinence from alcohol, the absence of any family members with genetic abnormalities, and any additional ionizing radiation exposure outside ambient radiation. They were all in good health and did not currently take any medications. Blood samples were taken between 7 and 9 AM from the antecubital vein and immediately divided into parts, first placed into the EDTA tubes for hematological analysis. The second part of the blood was placed in a clot activator, and later they were centrifuged (Hettich D-78532/Germany) at 3000 rpm for 30 minutes. Until they were tested, the sera were kept at -80°C (Sanyo, Ultra-Low Temperature, Japan).

2.5. BIOCHEMICAL ANALYSIS

2.5.1. Enzymatic activity

The activities of SOD, GPX, Catalase, Total antioxidant capacity represented by TAC, and the Human Carcinoembryonic Antigen (CEA) ELISA Kit were measured using the commercially available kits at My BioSource ELISA Test Kits, USA, subsequent the constructor's advices.

2.5.2. Carcinoembryonic Antigen (CEA)

The serum levels of CEA were determined using an ELISA assay kit (My BioSource ELISA Test Kits, USA) as per the guidelines provided by the manufacturer.

2.5.3. Liver function test parameters

Serum AST, ALT, and ALP levels and Total bilirubin levels were measured to assess the liver function tests. All of these biochemical assays were done using a fully automated biochemistry analyzer (Cobas, model BT35i, Japan) at the central lab belonging to Jimhury Hospital in Erbil city.

2.5.4. Complete Blood Count (CBC) Test

For CBC tests, the obtained blood was well mixed and run through the Abacus+ and Medonic machines. In this study, six CBC parameters were taken into account and examined across all groups: hemoglobin HGB (g/dL), white blood cells WBC ($10^{\wedge 9}$/L), platelet count PLT ($10^{\wedge 9}$/L), hematocrit (HCT) in %, and red blood cells RBC ($10^{\wedge 12}$/L).

2.6. Statistical analysis

The data were statistically analysed using social science-specific statistical software (SPSS, version 28), and the mean ± standard error of the mean was used to show the results. Based on the Shapiro-Wilk and Kolmogorov-Smirnov tests for normality, the data had displayed a normal distribution. Thus, the parametric test ran on all the data that was available. The outcomes were scrutinized using a one-way analysis of variance (ANOVA). The post-hoc Duncan test was used to compare groups. Values were considered significantly different if $p < 0.05$. The study utilized Pearson correlations and linear regression analysis to investigate the relationships between age, indoor radon levels, antioxidant levels, and the annual effective dose. The data that was gathered demonstrated a parametric distribution.

3. RESULTS AND DISCUSSIONS

3.1 Anti-oxidant activates

Individuals in the case group and those in the control group did not have significantly different ages, according to statistics. Average SOD, GPX, Catalase, and TAC activities were 227.54±10.32 U/ml, 19.55±0.68 mu/ml, 10.31±7.88 nmol/min/ml, and 0.39±0.21 mmol/l, respectively, in the study group. While in the control group, they were found to be equal to 204.12±7.68 U/ml, 18.62±1.05 mu/ml, 6.91±4 nmol/min/ml, and 0.28±0.14 mmol/l, respectively, as shown in Table 2 and Figure 2. According to statistical analysis the two groups' activities were very different from one another ($p < 0.001$).

Table 2: Oxidative stress, biochemical, and hematological changes in factory workers and non-factory workers in Erbil city

Group / Parameter	Control	Gypsum	Cement plant	Light weight block	Marble	Red brick 1	Crusher Stone	Concert block2	Averages of the study group
SOD	204.1± 1.71a	214.24± 0.57b	240± 2.53f	228.7± 0.61e	223.5± 0.35cd	240.5± 2.73f	227.1± 0.72de	218.7 ±0.53c	227.54±1.15
CEA	2.609± 0.30a	2.90± 0.41ab	6.305± 0.56cd	5.04± 0.52bcd	3.66± 0.65abc	6.44± 0.87d	4.86± 0.92bcd	3.135± 0.37ab	4.622±0.61
CATALASE	6.911± 0.92a	7.82± 1.41a	14.468± 3.19bc	9.39± 2.39ab	7.94± 2.85a	16.31± 2.99c	7.47± 1.03a	8.76± 1.72ab	10.31±2.21
GPX	18.62± 0.23a	18.90± 0.17ab	20.193± 0.08de	19.72± 0.66cd	19.20± 0.15abc	20.31± 0.17e	19.45± 0.14bc	19.02± 0.20ab	19.55±0.68
TAC	0.289± 0.03a	0.314± 0.06a	0.5085± 0.07bc	0.39± 0.08abc	0.34± 0.08abc	0.517± 0.07c	0.36± 0.04abc	0.32± 0.043ab	0.39±0.06
ALT	23.06± 1.08a	33.1± 3.31ab	43.6± 2.65bc	33.57± 5.22ab	32.3± 3.51ab	45.9± 8.17c	32.3± 3.21ab	30.36± 2.456a	35.87±4.10
AST	20.06± 0.68a	24.9± 0.99ab	28.4± 2.35de	25.7± 2.00cd	24.1± 1.12abc	32.0± 5.04e	25.4± 1.87bc	24.86± 1.22ab	26.48±2.08
ALP	60.20± 1.76a	76.5± 3.52bc	78.9± 4.61bc	77.00± 3.73bc	73.80± 4.97b	88.10± 5.90bc	83.40± 3.21bc	88.90± 8.33c	80.94±4.89
Total bilirubin	0.403± 0.04a	0.448± 0.06a	0.700± 0.15a	0.64± 0.05a	0.50± 0.06a	0.65± 0.17a	0.43± 0.09a	0.49± 0.04a	0.55±0.09
WBC	7.615± 0.38b	7.20± 0.51b	6.950± 0.32ab	7.26± 0.43b	5.77± 0.40a	7.09± 0.53ab	6.75± 0.22ab	7.12± 0.36ab	6.87±0.39
RBC	4.97± 0.08a	4.94± 0.09a	4.865± 0.10a	4.90± 0.085a	4.93± 0.081a	4.81± 0.55a	4.89± 0.12a	4.94± 0.11a	4.89±0.16
HBG	14.58± 0.14a	14.44± 0.21a	13.97± 0.22a	14.19± 0.42a	14.16± 0.23a	13.90± 0.11a	14.33± 0.38a	14.41± 0.13a	14.2±0.24
HCT	44.25± 0.44a	44.13± 0.45a	43.06± 1.00a	43.37± 0.63a	43.90± 0.90a	42.48± 0.79a	43.92± 0.80a	44.07± 1.12a	43.56±0.81
PLT	208.8± 7.83a	207.0± 9.23a	198.0± 11.42a	202.0± 12.25a	203.1± 10.71a	195.1± 12.68a	204.0± 8.50a	205.6± 8.50a	202.11±10.47

The different letters on bars mean significant and the same letters on bars mean no significant difference. The data represented mean ± SEM *P<0.05 considered a significant difference according to ANOVA followed by post hoc, Duncan test

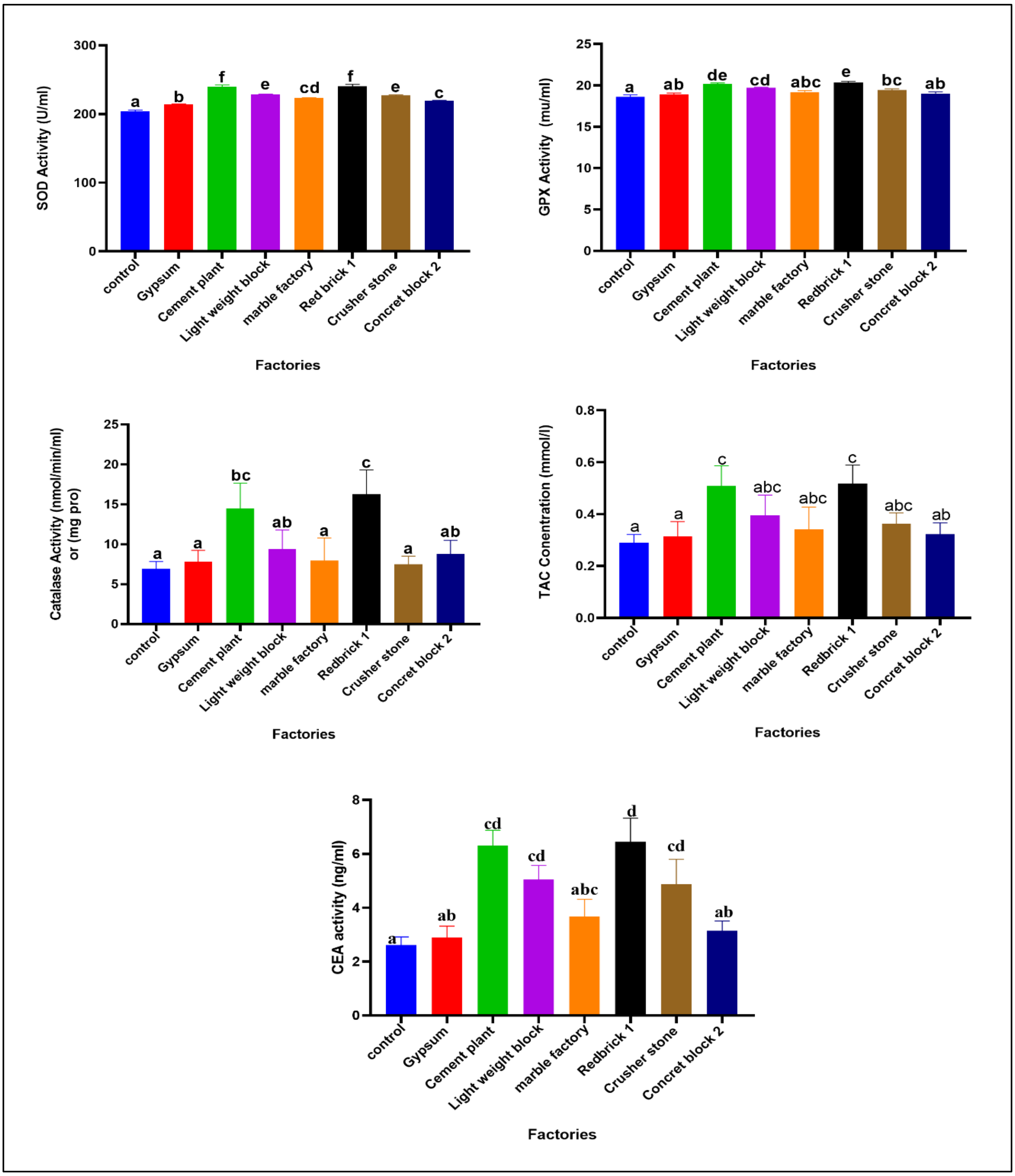

Figure 2: Antioxidant levels and CEA concentrations among different groups. The different letters on bars mean significant and the same letters on bars mean no significant difference.

According to Table 3, Pearson analyses of the case study group revealed a strong correlation between enzyme activities, the quantity of radon inside, and the effective annual exposure. The linear regression analysis illustrated in Figures 3, and 4 showed that GPX and catalase activity increased in proportion to SOD activity. Moreover, it is important to highlight that the same pattern has been observed in the control group, where the activity of GPX has shown a proportional rise alongside SOD activity. A strong correlation coefficient of 0.914, as shown in Figure 5, indicated that the observed association between the variables was very significant. SOD enzymes split o_2^- into two constituents, H_2O_2 and O_2. CAT and GPX break down the hydrogen peroxide produced by this process as well as from other sources. CAT catalyzes the conversion of H_2O_2 into H_2O and O_2, whereas GPX uses GSH as a substrate to catalyze the removal of H_2O_2. Therefore, increases in SOD activity, which would then increase GPX and CAT activity, may be a sign of levels. There is a substantial relationship between GPX and SOD activity in erythrocytes (Ramadhani et al., 2021). By using statistical analysis, specifically the Pearson correlation, which revealed a significant correlation (p <0.001), it was possible to determine the impact of age on antioxidant activities within the case study groups as shown in Table 3. Earlier studies have demonstrated that age affects GPX and SOD activity (Ceballos-Picot et al., 1992). Saraymen et al. also identified a noteworthy confident relationship between age and SOD activity from both male and female patients. Only females demonstrated a statistically significant association among age and enzyme activity in GPX (Saraymen et al., 2003).

Table 3: Person correlation analysis between radon concentration, annual effective dose, and age as independent variables with each antioxidant, liver function test, and hematological parameters as dependent variables in different factory workers in Erbil city.

Parameter	**Correlation coefficient** / **P value**	**Radon concentration ($Bq.m^{-3}$)**	**Annual effective dose ($mSv.y^{-1}$)**	**Age(y)**
SOD activity U/ml	r	0.845	0.844	0.685
	P	0.000	0.000	0.000
CEA activity (ng/ml)	r	0.478	0.77	0.399
	P	0.000	0.000	0.001
Catalase activity nmol/min/ml	r	0.324	0.325	0.269
	P	0.00	0.00	0.05
GPX activity(mu/ml)	r	0.688	0.687	0.482
	P	0.000	0.000	0.000
TAC concentration mmol/l	r	0.260	0.259	0.058
	P	0.05	0.05	>0.05
ALT(U/L)	r	0.263	0.264	0.231
	P	0.05	0.05	0.05
AST(U/L)	r	0.111	0.112	0.105
	P	>0.05	>0.05	>0.05
ALP(U/L)	r	0.011	0.010	0.034
	P	>0.05	>0.05	>0.05
Total bilirubin (mg/dl)	r	0.201	0.201	0.121
	P	>0.05	>0.05	>0.05
WBC (10^9/L)	r	-0.113	-.0.112	-0.013
	P	>0.05	>0.05	>0.05
RBC (10^12/L)	r	-0.114	-0.114	-0.154
	P	>0.05	>0.05	>0.05
HGB(g/dL)	r	-0.304	-0.303	-0.154
	P	0.01	0.01	>0.05
HCT (%)	r	-0.216	-0.216	-0.194
	P	>0.05	>0.05	>0.05
PLT (10^9/L)	r	-0.134	-0.133	-0.068
	P	>0.05	>0.05	>0.05

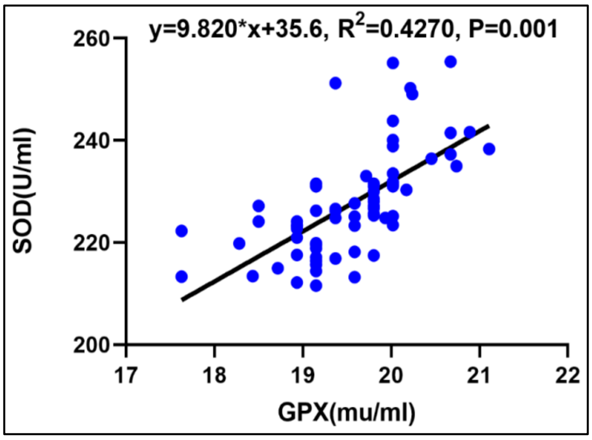

Figure 3: Correlation between SOD and GPX activity in the case study group

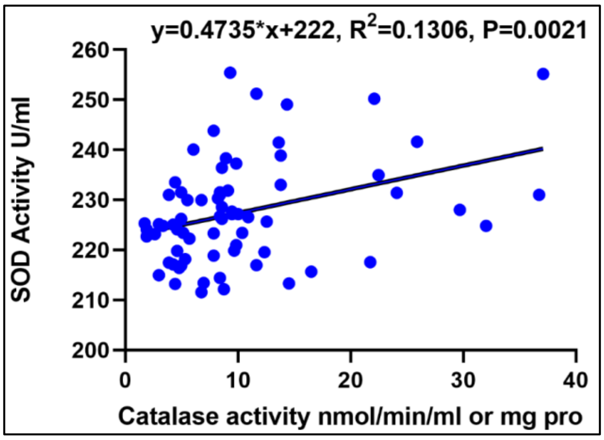

Figure 4: Correlation between SOD and Catalase activity in the case study group

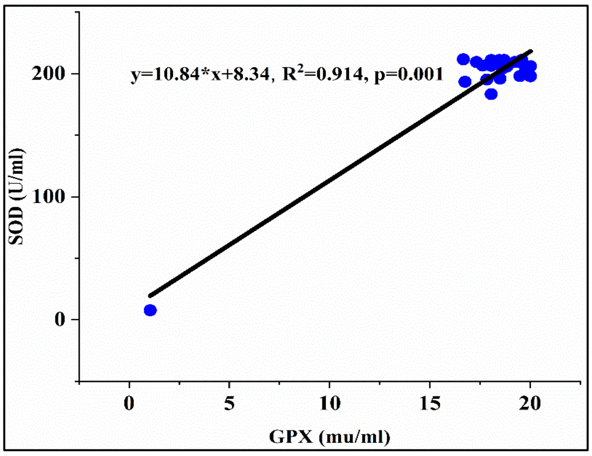

Figure 5: Correlation between SOD and GPX activity in the control group

To lower the number of unpaired electron compounds and stop ROS from damaging cells, aerobic organisms need the first-line antioxidants SOD and CAT (Su et al., 2018). The weighty alteration in SOD activity between groups is consistent with the findings of previous researchers. Su et al. (Su et al., 2018) discovered a significant increase in serum SOD activity among residents of Yangjiang, China, which has a high level of background radiation, compared to residents of locations with low levels of background radiation.

In animal models, equivalent findings were also made; Rats encountering radon at high levels show an increase in SOD activity in numerous organs (Ma et al., 1996, Kataoka et al., 2011, Kataoka et al., 2016, Kataoka et al., 2012, Mitsunobu et al., 2003, Yamaoka et al., 2004, Yamaoka et al., 2005). However, according to research by Eken et al., in Turkey, there are drastically higher levels of the SOD, GPX, and catalase compared to the control group (Eken et al., 2012). People who live in places with a lot of background radiation have higher levels of endogenous antioxidants like SOD, CAT, and GPX. This is one of the main ways that cells protect themselves during the radio-adaptive response (RAR) (Ramadhani et al., 2018). The present results demonstrated that individuals exposed to varied levels of interior radon had significantly different SOD, CAT, CEA, and GPX activities as compared with the control group. Even though the research group's changes in TAC concentration were more pronounced than in the control group. The significant change in TAC in the current study is comparable with the findings of Kuciel-Lewandowska et al. (2018a), which described the modifications made to the integrated antioxidant system in osteoarthritis patients receiving radon therapy. While it is contradictory to the findings of Nie et al. (2012). The shift in TAC concentrations in the study group may have been caused by small dosages of ionizing radiation from radon disintegrating (Kuciel-Lewandowska et al., 2018b). Given the importance of ROS conversions in disease development, it is reasonable to infer that an increase in the system's overall antioxidant capacity could be responsible for radon's toxic effects. Radon stimulates this process, which also generates free radicals.

To attain metabolic equilibrium and boost its ability to defend itself, the body stimulates a number of metabolic pathways as well as the endocrine system. The motivation of the mechanism with modest amounts of ionizing particles, however, has raised severe concerns in several scientific groups. The issue may arise from a lack of a thorough examination of radiation hormesis, which is thought to be the beneficial element that kick-starts the body's repair processes (Kuciel-Lewandowska et al., 2018b). A statistical analysis was done across four different radon levels, from low levels (>50 $Bq.m^{-3}$) to high levels (150 $Bq.m^{-3}$), to see how the concentration of radon affected the parameters that were observed in the study group.

The findings of the study indicate a considerable increase in enzymatic activities as the concentration of radon increases ($p < 0.001$), particularly when the radon levels exceed 150 $Bq.m^{-3}$. As shown in Table 4, there was a strong connection between radon concentration and their activities. As the radon level increases, the antioxidant levels also increase, especially in the red brick 1 and cement workplaces. This is because the powder created throughout the squeezing processes of making construction ingredients causes staff in this field to breathe more radon. In contrast, this could also be brought on by consuming substances containing radon and breathing air that has been contaminated with radon in the environment and industrial settings. Additionally, a statistically substantial variance in these levels was noticed, especially when compared to other factories. The firms in those factories often leave their doors and windows accessible the majority of the time to let heat and radon escape, which lowers the amount of radon that employees inhale (Othman et al., 2022).

Table 4**:** Impact of Radon concentration on some Oxidative stress, biochemical, and Hematological parameters in different factory workers in Erbil City

Radon concentration / **Parameters**	**>50 ($Bq.m^{-3}$) Radon concentration**	**50-100 ($Bq.m^{-3}$)**	**101-150 ($Bq.m^{-3}$)**	**>150 ($Bq.m^{-3}$)**
SOD	214.24±0.5707a	222.94±1.058b	230.73±1.5377c	240.48±2.732d
CEA	2.900±0.4154a	4.002±0.5264ab	5.0047±0.3826bc	6.447±0.8774d
CATALASE	7.8211±1.418a	8.1191±0.992a	10.602±1.661a	16.312±2.995b
GPX	18.906±0.1717a	19.239±0.1294a	19.706±0.09702b	20.317±0.1721c
TAC	0.314±0.0572a	0.3426±0.0297a	0.415±0.04683ab	0.5600±0.0775c

ALT	33.10±3.308a	31.33±1.981a	36.49±2.388ab	45.90±8.1737b
AST	24.90±0.9938a	25.13±1.090a	26.066±1.089a	32.00±5.042b
ALP	76.50±3.528a	86.15±4.389a	74.91±3.4793a	88.10±5.900a
Total bilirubin	0.448±0.0581a	0.4648±0.05353a	0.6153±0.05874a	0.6500±0.1765a
WBC	7.20±0.5151a	6.935±0.2124a	6.660±0.2479a	7.090±0.5344a
PLT	207.00±9.234a	204.80±7.296a	201.033±6.4078a	195.1±12.683a
RBC	4.942±0.9376a	4.923±0.0813a	4.9007±0.0519a	4.810±0.0555a
HGB	14.44±0.2151a	14.37±0.1969a	14.106±0.1728a	13.90±0.1183a
HCT	44.13±0.4533a	43.995±0.6743a	43.443±0.4840a	42.48±0.7966a

The different letters on bars mean significant and the same letters on bars mean no significant difference. The data represented mean ± SEM *P<0.05 considered a significant difference according to ANOVA followed by post hoc, Duncan test

3.2. Carcinoembryonic Antigen (CEA) concentration

The serum level of CEA for the case study group was found to be equal to 4.62±2.38 ng/ml, while that for the control group was 2.61±1.30 ng/ml. The statistical analysis showed that a substantial disparity between the two groups was found (p <0.001), as shown in Table 2 and Figure 2. The results of this investigation demonstrated a statistically significant association between the levels of CEA biomarkers and radon (r=0.478, p<0.000). The results indicated a statistically significant correlation between the concentration of radon and the levels of CEA. As the levels of radon increase, there is a significant increase (p<0.005) in the likelihood of an increase in CEA levels, as shown in Table 4.

According to global cancer data research, radon is the biggest threat to non-smokers and the second-leading cause of lung cancer after tobacco use. One of the biggest health issues in the world is LC. According to estimates, the likelihood of LC formation rises by 16% for every 100 $Bq.m^{-3}$. Due to radon's detrimental effects over the long term and the products of its decay, the HRR group is at high risk of developing LC, making early detection crucial for the mitigation, identification, and treatment of LC (Autsavapromporn et al., 2021). The association between high background radiation levels and cancer can be clarified by looking at tumor markers in the local population. According to studies by Mortazavi et al. (2005), Ramsar is renowned for having very high levels of ambient radiation. A study of tumor markers in locals may offer some insight into how high background radiation levels affect cancer induction, even though epidemiological studies have not discovered a higher cancer rate in these areas (Tao et al., 2012, Nair et al., 2009). However, the high background radiation area (HBRA) group displayed statistically substantial rises (P< 0.05) when compared to the CEA in the normal background radiation area (NBRA) group. It was also found that there was a statistically significant link (P 0.001) between the levels of radon inside homes and the concentration of biomarkers for carcinoembryonic antigen (CEA) (Taeb et al., 2014). Also, the results of a study that looked at the serum carcinoembryonic antigen (CEA) biomarker for LC risk screening in high residential radon (HRR) and low residential radon (LRR) areas showed that serum CEA was noticeably higher in the HRR group (p ≤ 0.0004) than in the LRR group (Autsavapromporn et al., 2021).

3.3. Liver function test

As seen in Table 2 and Figure 6, ALT, AST, ALP, and total bilirubin tended to rise in comparison to the control group across all groups. Serum ALT activity significantly rose (P<0.001) in the cement and red brick1 factories to 43.6± 2.65 U/L and 45.9±8.17 U/L, respectively, as compared to the control group value of 23.06± 1.08 U/L, whereas it remained relatively unchanged in the other factories. Serum AST activity increased significantly in the cement,

lightweight block, and red brick1 factories as compared to the control group. Moreover, with regard to the control group, AST activity was higher in the study groups. Statistical analysis revealed that serum ALP activity was increased as compared to the control group (P<0.001). As compared to the control group, total bilirubin activity did not increase significantly (P>0.05).

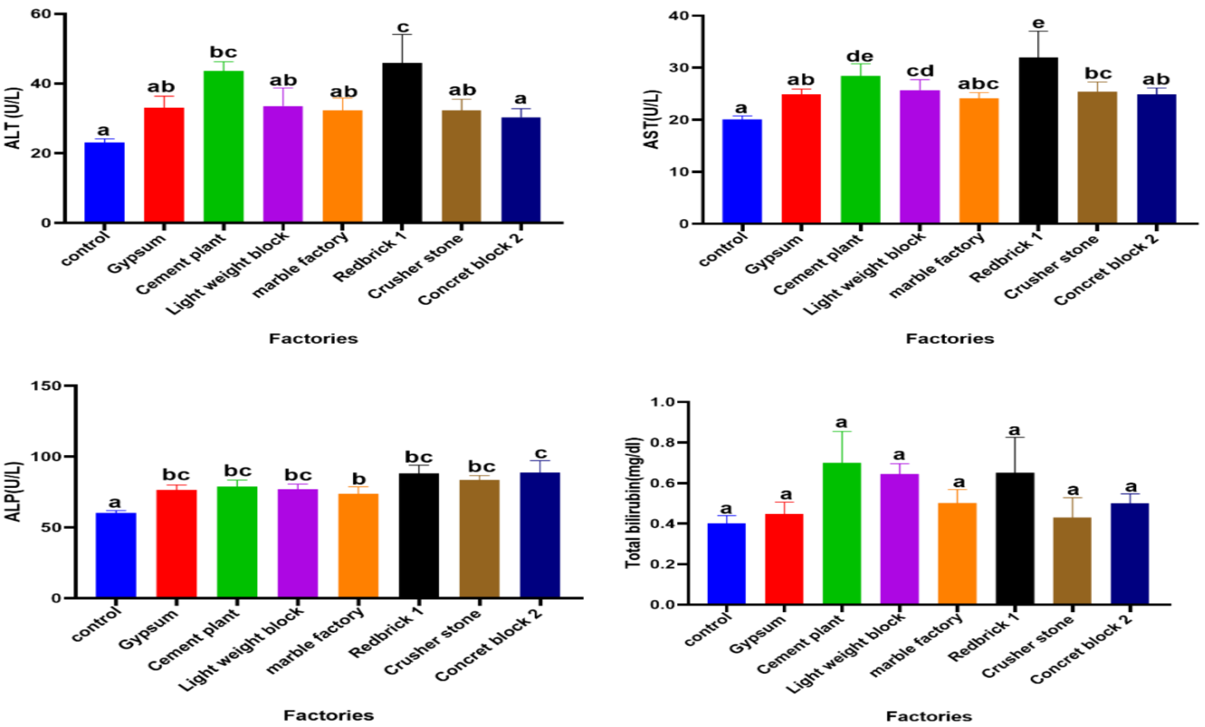

Figure 6: Liver function test for the studied factory workers and control group. The different letters on bars mean significant and the same letters on bars mean no significant difference.

The present results showed that radon concentration increased ALT activity in a radon concentration-dependent manner (r=0.263 and p <0.05), while AST activity was changed in a non-significant radon-dependent manner (r=0.011 and p >0.05). Also, the impacts of radon level on ALP activity were insignificant in a dose-dependent manner (r=0.011 and p >0.05). While the total bilirubin showed a non-significant radon-dependent manner (r=0.201 and p >0.05) as shown in Table (3). The statistical analysis demonstrated a significant correlation between liver function tests and radon concentration, particularly when the radon level reaches 150 $\mathrm{Bq.m^{-3}}$, as shown in Table 4.

The amount of radon-emitted ionizing radiation changed the activities of ALT, AST, and ALP in the serum compared to the control group. The current result is consistent with Ali et al., who concluded that when rats were exposed to γ-irradiation, which is ionizing radiation, there was a substantial rise in ALP, ALT, and AST levels (Ali et al., 2012). The liver, a primary organ involved in hemopoiesis, is extremely vulnerable to radiation injury. Free radicals produced from oxygen, such as O_2^- and OH, are causing tissue injuries (Hossain, 2000). Recent research has demonstrated that excessive levels of reactive oxygen species (ROS) and oxidative stress directly cause cellular and liver damage, with the liver being the primary target. Primary liver cells destroyed by oxidative stress are parenchymal cells (Li et al., 2015).

The serum ALT, AST, and ALP levels are general markers for hepatic toxicity. According to projections, the destruction of organs during exposure to ionizing radiation is linked to oxidative stress. When the liver is damaged from any cause, such as cirrhosis or hepatitis, the levels of these enzymes increase rapidly. In the metabolism of proteins and amino acids, transaminases are essential. They are discovered in the cells within the body, and at the time of sickness or injury influenced by these tissues, they enter the bloodstream. Some studies showed a substantial increase in liver enzyme activity (ALT and AST) after gamma irradiation (Abdelhalim and Moussa, 2013, Maulood et al., 2015).

The elevation of the liver enzymes in the current study may result from the increase in membrane permeability that occurred as a result of the increased creation of free radicals (Hoffmann et al., 2005).

It is well known that radiation can increase aminotransferase activity in blood serum by causing damage to hepatocyte cell membranes. This renders the cell membranes more permeable and makes it easier for cytoplasmic enzymes to exit the cells, thereby increasing aminotransferase activity (Ali et al., 2012).
In this study, ALT, AST, total bilirubin, and ALP levels increased significantly. This could be due to the rapid movement of these enzymes from the cytoplasm into the blood after the plasma membrane was ruptured and the cell was damaged. Ionizing radiation increases the activity of free radicals, as indicated by the elevated levels of liver indicator enzymes in serum, which indicate that radicals have caused lipid peroxidation in the cell membranes of the liver (Kafafy, 2000, Ramadan et al., 2001, Nada, 2008). Free radical production is thought to be the primary factor contributing to the negative outcome. These free radicals combine with cellular lipids and proteins to cause protein carbonylation and lipid peroxidation, which alter the structure of biomembranes and cause the liver to lose its structural integrity as well as its ability to carry out metabolic functions (Güven et al., 2003).

3.4. Hematological parameters

Figure 7 and Table 2 both display hematological profiles. The parameter that showed the most substantial impact on workers working in the marble sector, as compared to the control group, was the reduced WBC (P<0.001). Low PLT was the second-most-impacted metric. The other variables, however, between the research group and controls were not substantially different. The statistical analysis of the study group revealed a decline in hemoglobin levels across all factories. When linked to the control group, the WBC parameter experienced a statistically significant decrease in the study group, while the RBC and HCT parameters did not change significantly as compared to the control group.

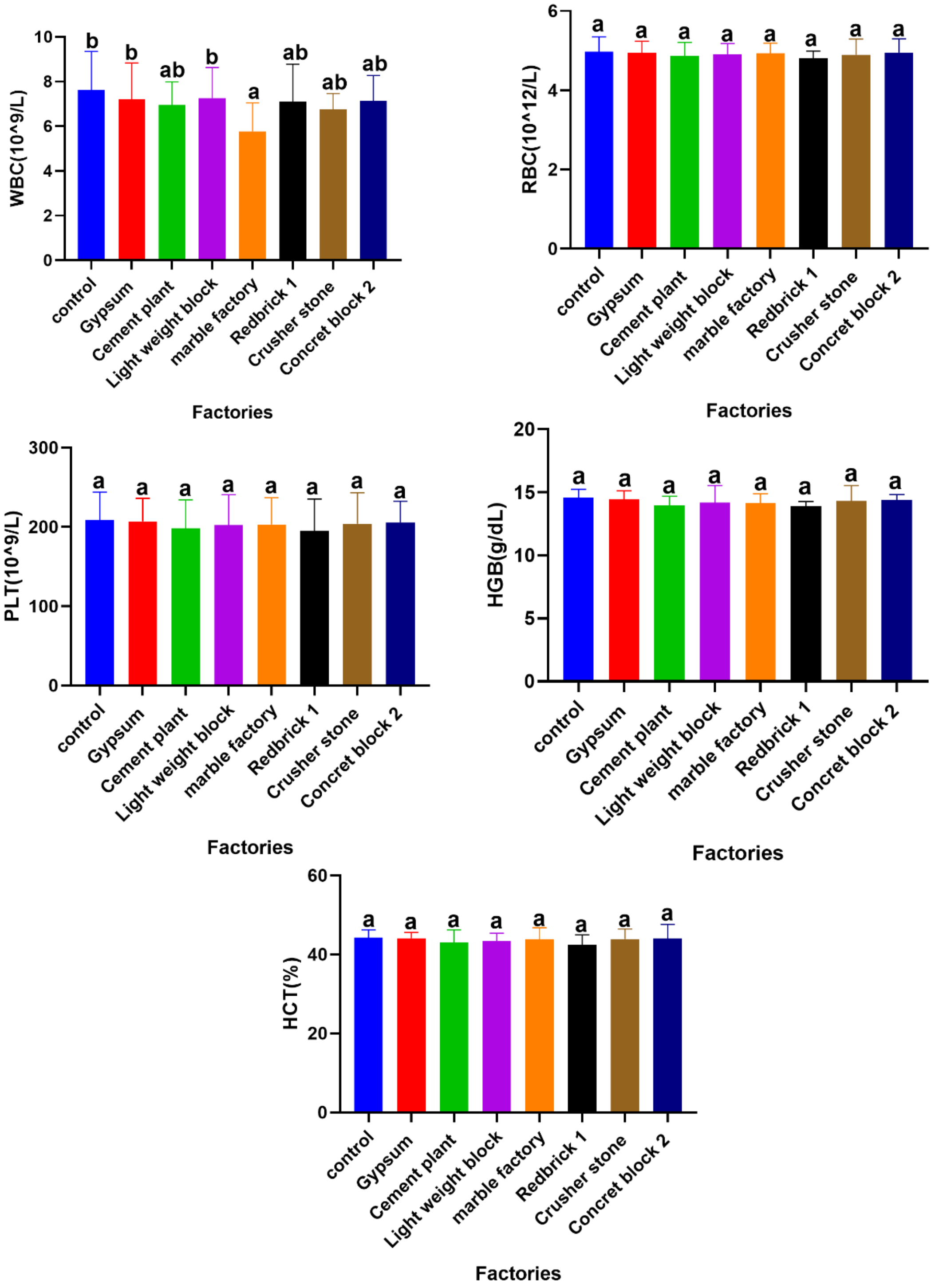

Figure 7: Hematological parameters for the studied factory workers compared with the control group. The different letters on bars mean significant and the same letters on bars mean no significant difference.

Hematological parameters and indoor radon concentration, or annual effective dose, did not significantly correlate (P>0.05), according to Pearson and Spearman analyses, in the case study group, as shown in Table 3. Also, it exhibited a non-significant connection (p>0.05) with increasing levels of radon, as indicated in Table 4. On the other hand, the decrease in PLT count in the study group wasn't significantly observed as compared to the control group (P>0.05). The number of platelets has decreased as a result of the alpha particle deposition, which is caused by radon daughters, and the degree of symptom intensity is influenced by a number of variables, including alpha particle energies, total dose, dose rate, dose distribution, and bodily vulnerability to radiation. The decrease in PLT in the study group is comparable with the results of (Ismail et al., 2011, Shahid et al., 2015).

The results obtained here revealed a decrease in HGB in the research group in comparison to the control group, in agreement with the results of Ismail et al. (2011). Because radon is a strong stressor that causes the body to produce free radicals, hemoglobin levels decreased. This was explained by the fact that low-dose alpha radiation is the primary cause of metabolic changes. One possible mechanism is radiation hormesis, which activates hemoglobin. Although hemoglobin's foremost role is to convey oxygen, it also catalyzes free-radical reactions and lowers the production of ROS (Rifkind et al., 2004). Exposure to ionizing radiation causes a reduced reaction in the circulating hematopoietic system, which can cause mature blood cells to undergo apoptosis. According to a study, exposed workers' mean total white blood cell counts were substantially lower than those of the controls (Caciari et al., 2012).

The environment and occupational exposure to tiny but persistent levels of ionizing radiation increase the health risks for workers (Milacic and Simic, 2009). Similar research was done to look at blood count parameters in people who live and work in low-ionizing radiation environments. Consumed doses inhibit the capacity of hematopoietic stem cells to self-renew (Milacic, 2008).

This study's findings must be viewed in light of a few limitations. Our study cannot conduct in vivo studies to evaluate how radon inhalation affects workers' respiratory systems. Women couldn't work in the field; therefore, the study only recruited men. To determine gender effects on findings, this was the first observational study to investigate serum CEA as a lung cancer biomarker in Erbil's indoor radon exposure area. Long-term studies are needed to prove blood CEA's prognostic efficacy in high-radon areas. Additional research is needed to confirm the results of this study.

CONCLUSION

This study looked at how inhalation of radon affected the antioxidant functions, biochemical parameters, and hematological indices of workers in a building materials factory in Erbil. The statistical analysis showed that the case study group had significantly higher antioxidant activity and CEA levels than the control group. There was a strong link between enzymatic activity, indoor radon concentration, and annual effective dosage for the case study group, as shown by Pearson and Spearman analyses. The result indicates a significant correlation between CEA biomarkers and radon levels ($r = 0.478$, $p<0.000$). Additionally, radon directly boosted ALT activity. The study found that there was no substantial effect of radon levels on AST activity. Radon dose-dependently affected ALP activity but was insignificant. Radon exposure had a weak effect on the total bilirubin. The most important CBC measure, white blood cell count (WBC), dropped significantly in the case study group compared to the control group. Platelet count reduction had the second-greatest impact. Other CBC parameters did not differ between the study and control groups. The study found that indoor radon affects CEA, liver function, CBC, and enzymatic activities. According to the study, these traits can be used as biomarkers to track radon harm to employees and residents. This study can overcome epidemiology's limitations in radon-rich places in Erbil to determine cancer prevalence. Tumor indicators may help regulators decide whether to limit Erbil exposure in high-background radiation areas. Therefore, it is recommended that the proprietor of the factory take measures to improve the ventilation system, decrease the duration of working hours, and enforce the use of protective masks. These actions are necessary in order to prevent the build-up of ^{222}Rn and its progeny. The study suggests that in any contaminated area of Kurdistan, addressing possible rising indoor radon pollution as a significant public health issue should be given top priority.

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