

Occupational Exposure of Diagnostic Technicians to X-Ray May Change Some Liver Functions and Proteins

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ABSTRACT

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Introduction: The most common impact of X-ray is the induction of cancer after chronic exposure. The current study was conducted to investigate the effects of low X-ray doses on some liver functions and proteins among diagnostic technicians working at Kirkuk hospitals, Kirkuk, Iraq. To this purpose, the parameters, such aspartate aminotransferase (AST), alanine aminotransferase (ALT), total protein, albumin, globulin, serum ferritin (s.ferritin), malondialdehyde (MDA), and glutathione (GSH) were measured in this study.

Material and Methods: In total, 20 male diagnostic technicians with a mean age of 39.55 ± 10.02 years participated in this study. On the other hand, 20 male healthy controls with a mean age of 39.9 ± 10.29 years were selected from outside of the hospitals. Five ml of blood was taken from each individual (technicians and controls). All parameters were measured with their own techniques.

Results: According to the results, significant increase ($p < 0.001$) was observed in the levels AST, ALT, and s.ferritin; however, there were remarkable decreases in the values of MDA, total protein, albumin, globulin, and GSH ($p < 0.001$) among diagnostic technicians, compared to the control group.

Conclusion: Based on the results, it was revealed that chronic exposure to low X-rays doses from conventional X-ray machine may change significantly the values of ALT, AST, s. ferritin, MDA, total protein, albumin, globulin, and GSH in diagnostic technicians who are exposed to an overdose at their workplace. It is important to utilize radiation protection tools, hold training courses, and follow up the technicians to reduce the effect of radiation on these individuals.

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Introduction

People are exposed to physical, chemical, and biological agents. Through the physical agents, ionizing radiations can produce damage to molecular systems [1]. Moreover, early and late effects on normal tissues and organs are induced by ionizing radiation [2, 3], which is commonly used in therapy against diseases and in diagnosis for detecting abnormality in human body. Ionizing radiations has an important role in modern medicine [4].

The X-ray has been widely used in medicine to create images using different techniques such as computed tomography scan, fluoroscopy and radiography. The most common impact of X-ray is the induction of cancer after chronic exposure [5-7]. Georgieva S. et al.(2013) showed that ionizing radiations could form reactive oxygen species (ROS) and damage cellular components including proteins, lipids and DNA by direct or indirect mechanisms[8,9]. The X-ray interacts indirectly through water radiolysis mechanisms producing free radicals which cause oxidative stress [10]. The ionizing radiation gives rise to produce large amounts of ROS in the body and the imbalance between the production of ROS and antioxidant defense can result in oxidative stress [11].

Diagnostic technicians may be exposed to soft X-ray during their daily life especially those who do not apply radiation protection rules as it is observed during this study. It has been proved that there is an association between ionizing radiation and malignant diseases [12, 13], including various hepatic diseases presenting with tender hepatomegaly, hyperbilirubinemia and ascites [14, 15]. It has also been proved that ionizing radiation can induce hepatic dysfunction or liver cancer in patients without hepatic diseases who undergo radiotherapy [16-19]. The high doses of ionizing radiation can induce liver damage; however, the effects of chronic exposure to low doses of radiation on liver damage are not clear [20]. Bakshi, M.V. et al. (2015) showed that liver inflammation in male mice increased after being exposed to a single dose ranging from 0.02 to 1.0 Gy[21]. Although the liver was once believed to be relatively radioresistant, hepatic morphologic and functional alterations have been observed after radiation therapy [22, 23]. Furthermore, the studies revealed that soluble enzymes of rat liver were affected by X and gamma (Co-60) radiations [24]. A number of investigators reported alterations in the serum

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proteins of animals exposed to whole-body irradiation [25, 26]. Serum ferritin (s.ferritin) is one of the measured parameters in this study which is an iron (**Fe**) molecules stored as a porous protein capsule and plays a major role in iron storage in the liver, spleen and bone marrow.[27]. The accumulation or diminution of iron is associated the incidence of several diseases [28].

The other two measured parameters in the present study include malondialdehyde (MDA) and intracellular glutathione (GSH). The MDA is the last product of peroxidation and a major aldehyde product that is mutagenic in cells and could be used to assess cell damages [29, 30]. Moreover, GSH is a common antioxidant in the human body participating in the human defense system against oxidative damage. It has been reported that GSH level can be reduced by oxidative stress [31].

There are still controversies regarding the effects of low doses of ionizing radiation; as a result, the majority of our studies are focused on this field. In our previous studies it was found that ionizing radiations led to DNA damage and apoptosis. Furthermore, in our recently published, it was revealed that some hematological parameters in diagnostic technicians altered significantly after being exposed to low doses of X-ray [32, 33]. Accordingly, this study focuses on other molecules such as proteins, enzymes and antioxidants. With this background in mind, the current study aimed to investigate the effects of occupational exposure to X-ray on liver functions and proteins among diagnostic technicians who work at the department of radiology in Kirkuk hospitals, Kirkuk, Iraq through measuring alanine

aminotransferase (ALT), aspartate aminotransferase (AST), total proteins, albumin, globulin, s.ferritin, MDA, and GSH.

Materials and Methods

This study was conducted from August to September 2018. In total, 20 male diagnostic technicians with the mean age of 39.55 ± 10.02 years participated in this study. On the other hand, 20 male healthy individuals with a mean age of 39.9 ± 10.29 years were selected from outside of the hospitals and considered as the control group. Initially, the research objectives were explained to all participants, and they were informed of the voluntary participation in the study. Subsequently, 5 ml of blood was taken from each subject in two groups. The participants were non-smokers, had no disease, and consumed no medications before and during the study. Table 1 tabulated some characteristics of the technicians. All technicians had experiences of working with conventional X-ray machines which used a low X-ray dose for imaging.

The AST, ALT, total protein, and albumin were measured by a technique according to the instructions of manufacturer company kit Randox (Biolabo kits, France), whereas s.ferritin was measured using an enzyme-linked immunosorbent assay technique. Moreover, globulin was determined using the following equation:

$$\text{Globulin} = \text{total proteins} - \text{albumin}$$

The MDA was measured based on the colorimetric reaction with thiobarbituric acid using spectrophotometer (Unico company, USA) [34].

Table1. Technician Characteristics

ID	Age	Working hours/day	No. of servicing years	No. of patients diagnosed / day	Smoking	Presences of other diseases
1	30	8	5	10	no	-
2	45	8	22	13	no	-
3	24	8	3	5	yes	-
4	50	8	8	20	no	-
5	25	6	3	10	no	-
6	31	6	6	7	no	Hyper tension
7	40	6	12	10	no	-
8	46	3	17	10	no	-
9	37	6	10	10	no	-
10	28	4	6	8	no	-
11	51	3	21	7	no	Hyper tension
12	38	6	14	10	no	-
13	31	6	8	15	yes	-
14	53	4	23	5	no	-
15	46	4	17	10	no	-
16	37	6	12	10	no	-
17	29	6	9	13	yes	-
18	55	4	25	15	no	-
19	42	6	14	15	no	-
20	53	3	19	8	no	-

Furthermore, the GSH level was estimated by mixing a 2.3 ml buffer (phosphate buffer, H₂O₂ buffer) with 0.2ml of the sample. Subsequently, 0.5 ml of 5, 5-dithio-bis-(2-nitrobenzoic acid) was added and the mixture was analyzed using spectrophotometer [35].

The data were analyzed using a statistical Minitab program (Minitab 17, Minitab Company, and USA). One way analysis of variance was used to evaluate the statistical difference among the means values of the two groups. A P values less than 0.05 was considered statistically significant.

Results

Effects of occupational exposure to X-ray on Alanine aminotransferase, Aspartate aminotransferase, and s.ferritin

The results obtained from the evaluation of AST, ALT and s.ferritin in two groups (i.e., diagnostic technicians and control) are shown in Table 2 and Figure1. According to the results, there is an increase in the values of the three parameters under study ($p<0.001$). Moreover, the mean values of AST, ALT and s.ferritin were 56.2 ± 16.73 U/L, 64.27 ± 15.27 U/L, and 62.46 ± 9.01 ng/L in the diagnostic technician group, whereas the corresponding values were obtained at 15.75 ± 3.13 U/L, 15.5 ± 2.81 U/L, and 44.07 ± 3.01 ng/L in the control group respectively.

Table 2. Measured values of Aspartate aminotransferase, Alanine aminotransferase, and S.ferritin in two groups

Parameters	Groups	Control Mean \pm SD	Diagnostic technicians Mean \pm SD	P-Value
Aspartate aminotransferase (U/L)		15.75 ± 3.13	$56.2\pm16.73^*$	<0.001
Alanine aminotransferase (U/L)		15.5 ± 2.81	$64.27\pm15.27^*$	<0.001
S.ferritin (ng/L)		44.07 ± 3.01	$62.46 \pm 9.01^*$	<0.001

* Significant difference $p<0.001$

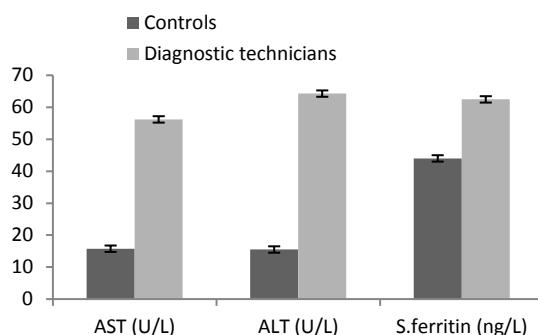


Figure1. Aspartate aminotransferase, Alanine aminotransferase, and S.ferritin values in two groups

Effects of occupational exposure to X-ray on total proteins, albumin, and globulin

As can be seen in Table 3, there is a significant decrease ($p<0.001$) in the amounts of proteins, albumin

and globulin a. The mean values of total protein, albumin and globulin were 5.93 ± 0.53 , 2.71 ± 0.32 , and 3.19 ± 0.25 mg/dl for the technicians group, respectively. Moreover, the corresponding values in the control group were estimated at and the values for the control were 7.33 ± 0.27 , 3.53 ± 0.16 , and 3.78 ± 0.13 mg/dl Figure2.

Table 3. Total protein, Albumin, and Globulin values in two groups

Parameters	Groups	Control Mean \pm SD	Diagnostic technicians Mean \pm SD	P-Value
Total protein (mg/dl)		7.33 ± 0.27	$5.93\pm0.53^*$	<0.001
Albumin (mg/dl)		3.53 ± 0.16	$2.71\pm0.32^*$	<0.001
Globulin (mg/dl)		3.78 ± 0.13	$3.19 \pm 0.25^*$	<0.001

* Significant difference $P<0.001$

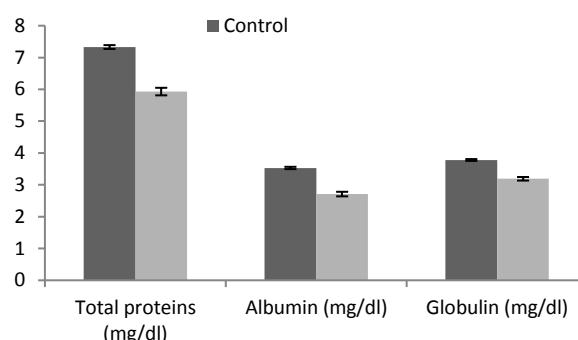


Figure 2. Total protein, albumin, and globulin values in two groups

Effects of occupational exposure to X-ray on the values of Malondialdehyde and Glutathione

Table 4 summarizes the values of MDA and GSH in the two groups. The MDA levels increased significantly ($p<0.001$) followed by a remarkable reduction in the GSH values ($p<0.001$). The mean values of MDA and GSH were estimated at 1.77 ± 0.27 and 1.24 ± 0.071 mol/l as well as 0.386 ± 0.028 and 0.442 ± 0.055 mol/l in the technicians and control groups, respectively. Figure3 represents the values of MDA and GSH in two groups.

Table 4. Malondialdehyde and Glutathione values in two groups

Parameters	Groups	Control Mean \pm SD	Diagnostic Technicians Mean \pm SD	P-Value
Malondialdehyde (mol/l)		1.24 ± 0.071	$1.77\pm0.271^*$	<0.001
Glutathione (mol/l)		0.442 ± 0.055	$0.386\pm0.028^*$	<0.001

* Significant difference $P<0.001$

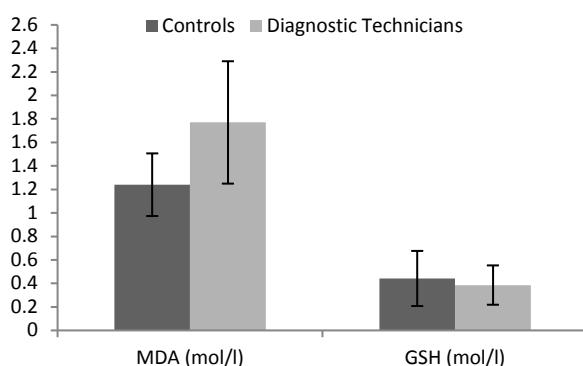


Figure 3. Malondialdehyde and Glutathione values in two groups

Discussion

The X-ray is vastly used for therapy and diagnostic purposes in medicine. Diagnostic technicians may be excessively exposed to low doses of X-ray during their professional life more than other people especially those who do not apply radiation protection rules as it was observed during this study. Since there is a dearth of research on the effects of low doses of ionizing radiation on liver functions, the present study aimed to investigate the risk of long term of X-ray on liver functions using ALT and AST measurements. According to the results both ALT and AST levels elevated significantly in the diagnostic technician group, compared with the control group. It was also showed that chronic exposure to radiation was a risk factor for liver injury; however, there was no association between accumulative radiation dose and hepatic injury [36]. CR Nwokocha et al. (2012) showed that the values of ALT and AST elevated significantly with increasing radiations after total body irradiations of rats to 1.27 Gy/minute as cumulative doses [37]. Furthermore Wei Cheng et al. (2015) observed that the levels of AST and ALT were elevated after irradiation of rats for 2 weeks [38].

The third measured parameter in the present study was s. ferritin. It has been shown that many diseases are correlated with iron overload or iron deficiency. S. ferritin has been described as a risk factor for veno-occlusive disease [39]. Similarly Zhe Feng et al. (2015) revealed a significant association between s. ferritin and colorectal cancer [40]. The determination of ferritin has been considered a suitable method for ascertaining the iron metabolism situation which provides a representative measure of body's iron reserves [28]. The diagnostic technicians obtained a significant increase in s.ferritin compared with the control group in this study. This increase may be due to oxidative stress and enzyme activity affected by the radiation. It has been reported that an increase in hepatitis and the direct effect of different inflammatory mediators such as acute-phase cytokines led to the changes in ferritin subunits [41-44].

Diagnostically, total serum protein measurement is remarkably important in assessing of state of an organism, and an increase in this parameter led to inflammatory processes and tissue dysfunction [37]. A

significant decrease in total protein, albumin and globulin was observed in the present study. In a study conducted by Jorn Ditzel (1962), after 1500 rad and 1000 rad of total-body X-irradiation of golden hamster the albumin fraction decreased; however, α_1 , α_2 - and β -globulin fractions increased [45]. In the same line E. S. Goranson et al. (1960) observed that animal exposure to supra-lethal total-body irradiation produced changes in a number of the serum components. The most striking change was the increase in the α -globulin component ($F\alpha_2$) [46]. The results of the current study were inconsistent with the findings of the two previous studies, which may be due to the differences in the amount of the absorbed dose. CR Nwokocha et al. (2012) also showed that serum proteins increased significantly with increasing radiation; moreover, serum levels of albumins increased significantly ($p < 0.05$) with the first to third radiation exposures followed by a reduction at the fourth cumulative dose exposure [37] which was in line with the results of the present study.

Oxidative stress induced by radiation may increase MDA, which is interesting for researchers, and the intracellular concentration of GSH can be used as an indicator of oxidative stress [47]. The results of this study showed alteration in both MDA and GSH. The value of MDA increased significantly, whereas there was a remarkable decrease in GSH level in the diagnostic technician group, compared to the control group. Decreased levels of GSH can be attributed to low dose of radiation which can induce oxidative stress. According to a study carried out by Meydan D.B. et al. (2011), ROS led to negative effects on the antioxidant defense by depleting the intracellular concentration of GSH [48]. In a similar vein Deger Y. et al. 2003 showed increased and decreased levels of MDA and GSH, respectively, after the irradiation of mice to 550 rad X-ray [49]. Based on the results of a study performed by Haitian Zhao et al. (2012), the levels of MDA increased followed by a reduction in the values of GSH in liver tissues of mice after irradiation to 5Gy of Co-60 [50]. The results of these two studies were in line with the finding of the present study. Oxidant damage to the mitochondria and myocyte membranes that could promote cell death due to membrane damage, which is termed "radiation induced apoptosis", may be due to a high level of MDA [51]. Liren et al 2010 showed an increase in the levels of MDA in the cardiac tissue of mice irradiated by gamma rays [52].

Conclusion

This study revealed that chronic exposure to low X-ray doses in diagnostic technicians who are exposed to radiation at their workplace may change significantly the values of ALT, AST, s. ferritin, MDA, total protein, albumin, globulin and GSH. The results also revealed significant associations between the aforementioned parameters and hepatic diseases. Since there is little evidence on the effects of low doses of ionizing radiation on these parameters, more studies are required to confirm the results. Moreover, it is recommended to

utilize radiation protection tools, hold training courses and follow up the technicians to reduce the effect of radiation on these individuals.

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