

Original Research Article

Estimation of Some Inflammatory Indices among Radiological Units Workers of Different Hospitals in Basrah Province -Iraq

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Abstract: **Background:** Exposure to ionizing radiations at work is an inevitable aspect of contemporary medical practice, especially in radiology units where radiology staff routinely operate with diagnostic imaging equipment like X-ray units. **Aim:** The present study aimed to determine the impact of X-ray radiations on X-ray technicians by measuring the levels of (CRP) C-reactive protein and (IL-6) Interleukin-6. **Methodology:** This study included a total of 75 male subjects. The study population comprised 50 X-ray technicians chosen randomly among the radiology departments in hospitals in Basrah province, Iraq. Concentrations of Serum CRP were measured by Genrui PA54 biotech kit and ELISA was used to quantify IL-6 concentrations. **Results:** The study showed that median serum IL-6 concentration was significantly higher ($p \leq 0.05$) in X-ray technicians 3.48 pg/mL (IQR:1.50-5.2) compared to control 1.10 pg/mL (IQR:1.10-1.50) as well as, the present results exhibited a significant increasing ($p \leq 0.05$) in the concentrations of CRP among X-ray workers 1.81 mg/L (IQR:1.31-4.10) compared to control (non-exposed) 0.91 mg/L (IQR:0.50-2.44) However, according to the years of work. The current data showed a significant increase ($p \leq 0.05$) in the concentrations of IL-6 in more than 10 years group 3.49 pg/mL (IQR:1.50-5.2) compared to group 1 (less than 10 years 1.49 pg/mL (IQR:1.10-3.49) while CRP didn't show any significant differences. **Conclusion:** Chronic occupational exposure to ionizing radiation was associated with increased circulating levels of IL-6 and CRP among X-ray technicians. The significant elevation of IL-6 in workers with long exposure duration suggests that cumulative radiation exposure may promote sustained inflammatory activation.

Keywords: Ionizing Radiation, X-ray, IL-6, CRP.

INTRODUCTION

Exposure to ionizing radiations at work is an integral aspect of contemporary medical practice, especially in radiology units where radiology staff are required to operate with diagnostic imaging equipment like X-ray units [1]. Although, it is widely acknowledged the benefits of medical imaging, the long-term effects of low dose radiation have also been of concern because of its delayed biological effects. These effects may not become effective immediately, but may have long-run effects on cellular homeostasis and immune-function [2]. The interaction of ionizing radiation with biological tissues mainly involves reactive oxygen species (ROS) generation. It should be noted that there is a very strong correlation between oxidative stress and the activation of inflammation [3]. This indicates that there is a complex interplay between exposure to radiation and the immune system. X-rays are high-frequency electromagnetic rays that can ionize atoms and molecules and are produced when electrons collide with a heavy metal target. The ionizing radiation is sufficiently energetic (100 eV-100 keV) to pass through living tissues, thus causing cellular disruption or functional disturbances [4].

Ionizing radiation causes a complex sequence of events that lead to systemic inflammation at a molecular level. Among them, a major one is the activation of Nuclear Factor-kappa B (NF- κ B) pathway, which is often triggered by secreted ROS, DNA double-strand breaks, induced by radiation. This activation results in the up-regulation of a number of cytokines involved in the inflammatory response, particularly Interleukin-6 (IL-6) [5]. Additionally, damage associated

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molecular patterns (DAMPs) have been released by damaged cells that interact with pattern recognition receptors on immune cells, leading to a perpetuated chronic inflammatory state, even at low occupational exposures [6]. Inflammation is a complex process which is a primary mechanism in the processes ensuring tissue integrity. However, chronic mild inflammation is increasingly recognized as increasingly an important risk factor for chronic diseases [7]. Among inflammatory biomarkers two most extensively studied ones are interleukin-6 (IL-6) and C-reactive protein (CRP). IL-6 is considered a multipotent cytokine which participates in regulating immune response, hemopoiesis and acute phase reaction. The second molecule, namely, CRP, is produced by the liver under the influence of IL-6 and is related to IL-6 quite closely in the process of inflammation [8].

Previous studies has been noted that the impact of ionizing radiation on the body can cause changes in the profile of cytokines and increase the level of inflammatory mediators. In this regard, for example, radiation workers with ionizing radiation can be characterized by a high concentration of IL-6 due to oxidative stress, which occurs as a result of radiation exposure and reduction in the functioning of the cells' signals. CRP was considered the most sensitive indicator of systemic inflammation in the population exposed to occupational and environmental risks [9]. On the other hand, there were inconsistencies in previous studies, particularly on low-level chronic exposure in this case [10], when it comes to radiology workers, the assessment of inflammatory biomarkers would serve as an readily available indicator for the main biological effect of the radiation exposure at the pre-clinical stage of the disease development process.

The biomarkers can be used as an indicator of occupational safety measures. Inflammatory markers such as IL-6 and CRP are becoming more widely used clinically and are important to assess the subclinical health risks of chronic low dose radiation exposure. International safety guidelines specify radiation doses but are not always aligned with the cumulative biological stress that can be expected from the long-term radiation exposure and cause cardiovascular and metabolic effects [11]. In Basrah, Iraq, the area of occupational radiation, there is a significant paucity of local data pertaining to their long-term effect on inflammatory profile among healthcare workers. To fill this gap in the literature, this study aims to assess the integrity of the health workers in hospitals within Basrah city at radiology units according to the specific environmental and occupational circumstances that may differ from one region to another and affect the biological outcomes [12-14]. Nevertheless, in developing countries such as Iraq, the lack of data is apparent, and the exposure levels might vary [13, 15]. This study aims to quantify the serum levels of IL-6 and CRP among X-ray technicians and a control group without x-ray exposure, examine the relationship between duration of occupational exposure and intensity of inflammatory response, and determine the efficiency of current and existing radiation protection measures to reduce systemic inflammation among X-ray technicians.

METHODOLOGY

Study Population and Design

This study included a total of 75 male subjects. The study population comprised 50 X-ray technicians (aged 24-50 years) randomly enrolled from the radiology departments (X-ray unit) of five hospitals in Basrah province, Iraq. Daily Hours of exposure to X-ray was 10.26 ± 4.89 hours they were recruited from the period between March 2023 to October 2023. Based on the duration of occupational exposure (years of work), the X-ray technicians were stratified into two subgroups: Group 1 (n=25) with less than 10 years of exposure and Group 2 (n=25) with more than 10 years of exposure. A control group consisting of 25 apparently healthy control with no occupational radiation exposure was included for comparison.

Inclusion Criteria

The study involved males X-ray technicians who were working in the radiology departments of the hospitals of Basrah province in Iraq and aged 24-50 years.

Exclusion Criteria

Exclusion criteria were participants with inflammatory conditions that might have influenced the results of interleukin-6 and C-reactive protein. Similarly, those who showed anemia, diabetes, heart disease, acute or chronic infections and in addition auto-immune and kidney disease were all excluded in order to impart greater accuracy to the results. Participants who were smokers or were taking anti-inflammatory drugs also were excluded.

Sample Collection and Processing

Venous blood samples 5 mL were collected from all 75 subjects (50 X-ray technicians and 25 control subjects) by venipuncture using sterile disposable syringes under aseptic conditions. The blood was immediately transferred into sterile plain tube and allowed to clot at room temperature for 30 minutes at 4000 rpm for 15 minutes. The separated serum was aliquoted into sterile microtubes (Eppendorf, Germany) and stored at -20° C.

Measurement of Interleukin -6 (IL-6)

Serum IL-6 concentrations were quantified using sandwich enzyme linked immunosorbent assay (ELISA kit) (Komabiototech, France) as per the instructions of the manufacture.

Measurement of C-Reactive Protein

The CRP was measured quantitatively by (Genrui PA54 biotech kit, China). This principle of this kit is based on producing a specific conjugation with CRP in the sample and an immunological complex of latex-antibody-CRP antigen, the specific CRP antibody is attached to the latex particles in this kit. The complex formation and the sample's CRP concentration are positively correlated. The specific protein analyzer can identify this immunological complex. Each detection kit is assigned a single magcard, and the reagents are pre-calibrated. Each unique calibration curve has been entered into the magcard.

Statistical Analysis

The Shapiro-Wilk test was used to determine was used to check the normality of data. Statistical Package for social sciences (SPSS) software version 25 was used. The data for IL-6 and CRP concentrations were not normally distributed and so the median and interquartile range (IQR:25-75%) were used to present these data. The Mann Whitney test was used to compare two independent groups, and the chi-square test (χ^2). A significant probability p -value was considered as 0.05 or less. The quantitative variables were evaluated in the form of mean \pm Standard Deviation.

RESULTS

The Shapiro-Wilk test demonstrated that IL-6 concentrations were not normally distributed in either group. Therefore, than Mann-Whitney U-test was applied. The median serum IL-6 concentration was significantly higher ($p \leq 0.05$) in X-ray technicians 3.48 pg/mL (IQR:1.50-5.2) compared to control 1.10 pg/mL (IQR:1.10-1.50) as in (Table 1).

Table 1: Serum IL-6 concentrations of the X-ray technician group and control group

Parameter	Subjects	n	Median (IQR: 25-75%)	p-value
IL-6 (pg/mL)	X- ray technicians	50	3.48(1.50-5.2)	0.002*
	Control	25	1.10(1.10-1.50)	

n= number of sample, *= Significant difference at ($p \leq 0.05$), IQR =Interquartile Range , IL-6 =Interleukin -6 , pg/mL =picogram per milliliter

The current data in (Table 2) showed a significant increase ($p \leq 0.05$) in the concentrations of IL-6 in group 2 more than 10 years 3.49 pg/mL (IQR:1.50-5.2) compared to group 1 (less than 10 years 1.49 pg/mL (IQR:1.10-3.49).

Table 2: Comparison of serum IL-6 concentrations (pg/mL) among X-ray technicians on the basis of years of work

Parameter	Duration of exposure	N	Median (IQR: (25-75%))	p-value
IL-6 (pg/mL)	Group 1 (< 10 years)	25	1.49(1.10-3.49)	0.02*
	Group 2 (> 10 years)	25	3.49(1.50-5.2)	

n= number of sample, *= Significant difference at ($p \leq 0.05$), IQR =Interquartile Range, IL-6 =Interleukin -6, pg/mL =picogram per milliliter

The present results exhibited a significant increase ($p \leq 0.05$) in the concentrations of CRP among X-ray workers 1.81 mg/L (IQR:1.31-4.10) compared to control (non-exposed) 0.91 mg/L (IQR:0.50-2.44) as in (Table 3).

Table 3: Comparison of serum CRP concentrations mg/ L between the X-ray technicians group with unexposed control group

Parameter	Subjects	n	Median (IQR: (25-75%))	p-value
CRP (mg/L)	X-ray technicians	50	1.81(1.31-4.10)	0.01*
	Control	25	0.91 (0.50-2.44)	

n= number of sample, *= Significant difference at ($p \leq 0.05$), IQR =Interquartile Range, CRP =C-reactive protein, mg/L =microgram per liter

(Table 4) According to the duration of occupational CRP concentrations between both groups didn't show any significant differences.

Table 4: Comparison of serum CRP concentrations (mg/L) of between two groups of X-ray workers on the basis of years of work

Parameter	Duration of exposure	n	Median (IQR: (25-75%))	p-value
CRP (mg/L)	Group 1(< 10 years)	25	1.68 (1.17-2.23)	0.38
	Group 2 (> 10 years)	25	1.71 (1.34-4.49)	

n= number of sample, *= Significant difference at ($p \leq 0.05$), IQR =Interquartile Range, CRP =C-reactive protein, mg/L =microgram per liter

DISCUSSION

X-ray equipment and other forms of radiation sources are used for diagnosing and treating illnesses in hospitals. The employees of hospitals working in the field of radiology, nuclear medicine, radiation oncology, and even some of the laboratories are well trained regarding the use of radiation equipment and radioactive sources. This is particularly because of the health dangers associated with radiations to this significant occupational group of the population [16, 17].

Thus, there was a statistically significant increase ($p \leq 0.05$) in IL-6 levels in the X-ray technician group compared to the control group. The reasons for such an increase in the process of mediators involved are complex and may be associated with higher levels of ROS (Reactive oxygen species), oxidative stress, DNA damage, and immune suppression caused by ionizing radiation [18]. The biological impact of ionizing radiation is induced either directly DNA damage or indirectly through ROS generation [19]. It has been proven that cell DNA damage contributes to the secretion of various cytokines that control immune responses such as IL-6 [20]. Based on our findings, we propose that low dose of radiation has the capacity to induce cellular damage – possibly through induction of ROS – and hence cytokine secretion through immune response. On the molecular level, NF- κ B is an important protein complex involved in immune response that is activated due to exposure to ionizing radiation [21]. NF- κ B moves into the nucleus of the cell after DNA damage from the radiation and stimulates the production of genes that code for pro-inflammatory cytokines, particularly Interleukin-6 (IL-6) [22]. This mechanism is invoked to account for the elevated levels of this cytokine under chronic low-level exposure, and that is because the cell stays in biochemical watch mode (SCR) [23].

The immune system was affected by radiation as a component of the body regulate the changes in the homeostasis and/or in its components. Epidemiologic studies over long periods show that ionizing radiation can cause dose-dependent deregulation of the immune system resulting in persistent inflammation and deregulation of cytokine production which is anticipated to cause both cancer and noncancerous diseases [18-24]. Some of the indicators of inflammation as adhesion molecules and cytokines that are increased by the radiation-induced oxidative stress, when they interact with cell surface markers trigger certain mechanisms and activate immune response. T helper 1 (Th1) lymphocytes that secrete pro-inflammatory cytokines (IL-6, IL-1 and TNF- α) are activated subsequent to irradiations, whereas T helper 2 (Th2) lymphocytes that secrete anti-inflammatory cytokines restore homeostasis [25].

In addition, there was a strong duration dependent effect for IL-6 with technicians working for over 10 years having significantly higher concentrations (3.49 pg/mL) than technicians working for less than 10 years (1.49 pg/mL). This time-dependent increase in inflammatory markers is in line with the results reported by Asl *et al.*, [25], which showed a dose-dependent link between prolonged ionizing radiation exposure and increased levels of IL-6 [26]. Likewise, Ahmad *et al.*, [27], showed that radiation exposure at work changes over time the circulating redox and inflammatory biomarker. Interestingly, although IL-6 did show significant increases that were duration dependent in the present study, there were no similar results for CRP based upon years of work. This difference could be due to the physiological kinetics of these biomarkers; IL-6 is an upstream primary cytokine directly influenced by chronic cellular stress and ROS production, while the baseline level of CRP may vary according to numerous transient physiological events [12-28]. This persistent high level of these pro-inflammatory cytokines highlights the need for ongoing biomonitoring because it can result in chronic inflammation, which can lead to a range of health issues for healthcare workers in the long term, such as cardiovascular diseases and radiation-induced cell damage [2-27].

The present study showed that there is a statistically significant difference between the median of serum concentration of C-reactive protein (CRP) of technicians occupationally exposed to ionizing radiation and the control group. The discovery is in line with modern research on occupational radiation-induced health effects, which shows that low-dose, chronic occupational radiation exposure triggers systemic inflammatory responses, including increased acute-phase reactants [26]. C-reactive protein is a sensitive systemic inflammatory marker that is produced mainly by hepatocytes stimulated by pro-inflammatory cytokines, mainly by interleukin-6 (IL-6) which is also significantly elevated in radiation-exposed workers [25]. These cytokines in turn activate the production of acute phase proteins by the liver such as CRP, which is part of the innate immune system response to any recognized signal of stress or damage to cells. The above indicated that CRP is sensitive in detecting subclinical inflammatory changes due to chronic exposure to low levels of

radiation even when the annual effective dose to the worker is still within the current internationally accepted limits of radiation safety [12].

The long-term increase in CRP among all workers exposed, irrespective of the length of exposure, indicates that, for workers exposed to radiation, even brief exposure can cause an acute inflammatory response that does not appear to increase with additional years of service [28]. This plateau effect has been seen in other occupational exposure studies, and it could be due to adaptive physiological mechanisms or to a new inflammatory homeostasis in the presence of low-level chronic stress [20, 21].

Limitations

There are a number of important limitations to this study that should be considered. Firstly, the small number of subjects (n=75) and their all-male population limit the generalizability of the results to female radiological workers, who may have different inflammatory reactions because of hormonal differences. Second, causality cannot be established as a result of the cross sectional design, and the associations between radiation exposure and higher inflammatory markers cannot be considered as causal. Thirdly, the use of years of occupational exposure was also used as a proxy for radiation dose instead of using dosimetric information from personal dosimeters or institutional records, thereby reducing the accuracy of dose-response analysis. Finally, the study failed to consider factors that may vary from one hospital to another, which could affect the amount of radiation to which technicians are exposed, such as differences among hospitals in radiation shields, equipment, and use of individual protective equipment.

CONCLUSION

The present study showed that the serum concentration of IL-6 and CRP was significantly higher in occupationally exposed X-ray technicians than in non-exposed controls. Technicians with >10 years of occupational exposure had significantly higher levels of IL-6 than those with less than 10 years, indicating that, long-term radiation exposure may have an inflammatory effect. These results suggest that chronic low-dose ionizing radiation can potentially play a role in the development of chronic systemic inflammation and emphasize the need for ongoing monitoring of the body of biomaterials and application of radiation protection measures by radiation workers.

Ethical Approval

The study was conducted after obtaining written approval from the Basrah Health Directorate to carry out the study in the Radiology Department. Verbal consent was also obtained from all participants in this study.

Conflict of Interest: The author declares that there is no conflict of interest in this article.

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