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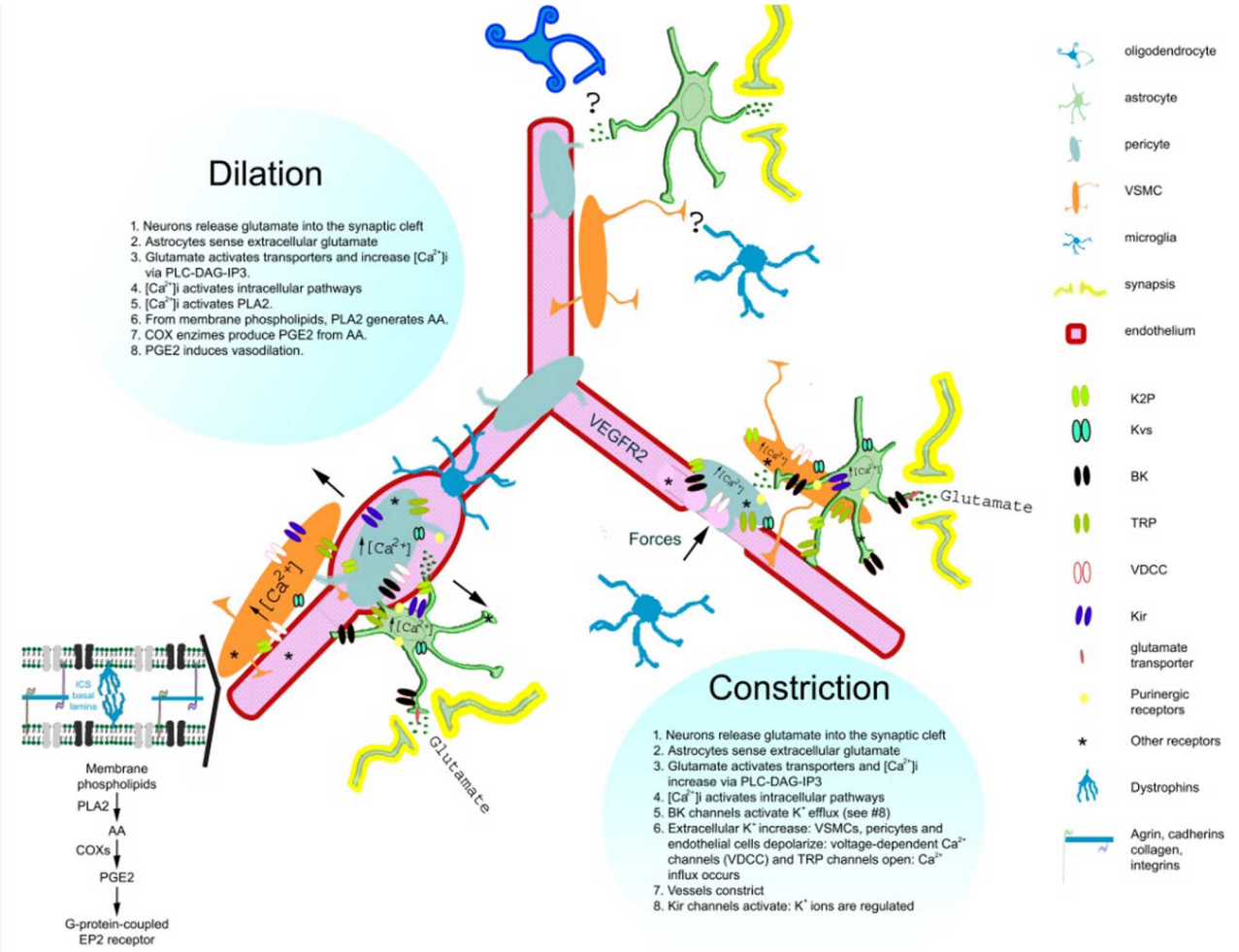

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AIM AND SCOPES
Journal of Cellular Neuroscience and Oxidative Stress is an online journal that publishes original research articles, reviews and short reviews on the molecular basis of biophysical, physiological and pharmacological processes that regulate cellular function, and the control or alteration of these processes by the action of receptors, neurotransmitters, second messengers, cation, anions, drugs or disease.

Areas of particular interest are four topics. They are;

A- Ion Channels (Na^+- K^+ Channels, Cl^- channels, Ca^{2+} channels, ADP-Ribose and metabolism of NAD^+, Patch-Clamp applications)

B- Oxidative Stress (Antioxidant vitamins, antioxidant enzymes, metabolism of nitric oxide, oxidative stress, biophysics, biochemistry and physiology of free oxygen radicals)

C- Interaction Between Oxidative Stress and Ion Channels in Neuroscience
(Effects of the oxidative stress on the activation of the voltage sensitive cation channels, effect of ADP-Ribose and NAD^+ on activation of the cation channels which are sensitive to voltage, effect of the oxidative stress on activation of the TRP channels in neurodegenerative diseases such Parkinson's and Alzheimer's diseases)

D- Gene and Oxidative Stress
(Gene abnormalities. Interaction between gene and free radicals. Gene anomalies and iron. Role of radiation and cancer on gene polymorphism)

READERSHIP

Biophysics	Biochemistry
Biology	Biomedical Engineering
Pharmacology	PhysiologyGenetics
Cardiology	Neurology
Oncology	Psychiatry
Neuroscience	Neuropharmacology

Keywords
Ion channels, cell biochemistry, biophysics, calcium signaling, cellular function, cellular physiology, metabolism, apoptosis, lipid peroxidation, nitric oxide, ageing, antioxidants, neuropathy, traumatic brain injury, pain, spinal cord injury, Alzheimer's Disease, Parkinson's Disease.

RESEARCH ARTICLE

J Cell Neurosci Oxid Stress 2021;13(2): 994-1003.

Effects of occupational exposure to ionizing radiation on oxidative stress and inflammatory markers in healthcare workers of a university hospital in Konya, Turkey

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List of Abbreviations;

***IR**, Ionizing radiation; **TNF,** Tumor necrosis factor; **TOS,** Total oxidant status; **IL,** Interleukin; **TAS,** Total antioxidant status; **OSI,** Oxidative stress index; **RNS,** Reactive nitrogen species; **ROS,** Reactive oxygen species; **DAMPs**, Damage-related molecular patterns; **TLR,** Toll-like receptors; **ROC,** Receiver operating characteristics.*

Abstract

Ionizing radiation (IR) has a wide area of use and its effects on human health have been discussed since its discovery. This study aimed to show oxidative stress and inflammation due to ionizing radiation exposure based on biomarkers in healthcare workers. This study was conducted with 172 people, who were exposed to IR in the work environment and those who did not have exposure to radiation. In this cross-sectional study, a data collection form was used to obtain data from the participants. In addition, blood sample was taken to measure their tumor necrosis factor (TNF)-alpha, total oxidant status (TOS), interleukin (IL)-10 and total antioxidant status (TAS) levels, and calculate their oxidative stress index (OSI) values. In the ionizing radiation group, 50% of the participants were men, the mean age was 35.91±7.07 years, and the mean duration of employment was 9.80±7.1 years.

The TOS, OSI, TNF-α and IL-10 values were higher and TAS was lower in the ionizing radiation group compared to the participants without exposure to ionizing radiation. Gender, smoking, alcohol use, presence of chronic diseases, regular medication use, antioxidant supplement use, and exposure to radiation for medical diagnosis and treatment within the last year did not affect oxidative stress and inflammation in the radiation workers. The cut-off values of the TOS, TAS, OSI, TNF-α and IL-10 biomarkers were also determined. Occupational low-dose long-term exposure to ionizing radiation was found to increase oxidative stress and inflammation.

Keywords: Ionizing Radiation; Oxidative Stress; TNF-α; Interleukin-10; Occupational Exposure

Introduction

Exposure to ionizing radiation (IR) causes damage by directly and indirectly affecting cells. Direct effects occur through the disruption of atomic structures by the generation of biological and chemical products while indirect effects are observed with the formation of reactive nitrogen (RNS) and oxygen species (ROS) that damage macromolecules, such as lipids, proteins and DNA through the radiolysis of the water molecule. The uncontrolled and excessive production of free radicals results in oxidative stress, which contributes to the pathogenesis of various diseases, including cancer, neurodegenerative disorders, liver damage, cardiovascular abnormalities, and diabetes mellitus (Arslan 2017; Tokaç 2018).

Oxidative stress occurs when the balance between the rate of generated free radicals and reactive metabolites referred to as RNS and ROS and the capacity of protective mechanisms called antioxidants is disrupted in favor of oxidants. IR can also impair mitochondrial functions by leading to permanent changes in nuclear DNA and mitochondrial DNA (Azzam et al. 2012; Chen et al. 2019; Sebastià et al. 2020; Tokaç 2018).

Defense systems created to prevent or reduce oxidative damage caused by reactive radicals are called antioxidant systems. Antioxidants enter into reactions and reduce oxidative stress by consuming molecular oxygen or decreasing its local concentration, removing prooxidative metal ions, trapping aggressive ROS, such as superoxide anion radical and hydrogen peroxide, scavenging chain initiating radicals, such as hydroxyl, alkoxyl, and peroxyl, breaking the radical sequence chain, or quenching singlet oxygen (Pisoschi and Pop 2015).

IR induces an immune response in tissues, causing inflammation. The resulting inflammation can damage various organs over years. Triggered inflammation is a complex process involving vascular injury, migration of leukocytes to the irradiated area, and release of immune system mediators. The response of normal tissues to IR is largely dependent on the radiation dose, and the incidence of vascular damage, hypoxia, and cell necrosis increases as the exposure dose increases. The effects of exposure to IR depend on the immune system response and the cytokine profile. The exposure of body cells to low doses of IR (less than 1 Gy) may produce an anti-inflammatory effect by triggering apoptosis rather than necrosis while exposure to higher doses of IR (more than 1 Gy) results in necrosis rather than apoptosis, causing inflammation (Yahyapour et al. 2018).

Although vascular damage and necrosis are responsible for the initiation of inflammation, other forms of cell death, such as apoptosis, autophagy, and senescence can also stimulate the inflammatory response in stressful conditions, such as exposure to high doses of IR. DNA damage and cell death that occur following exposure to high-dose IR (more than 1 Gy) result in the release of cellular contents, such as damage-related molecular patterns (DAMPs), with the most important being high-mobility group box 1, heat-shock proteinsanduric acid. Toll-like receptors (TLR) 2, 4, 5 and 9, which recognize the released DAMPs, play a central role in the activation of inflammatory pathways (Najafi et al. 2018; Roh and Sohn 2018; Yahyapour et al. 2018).

TLR stimulation activates intracellular signaling pathways, such as intracellular cyclooxygenase-2, mitogen-activated protein kinases, and nuclear factor-κB, thereby triggering the release of interleukin (IL)-1, IL-6, IL-8, IL-33, interferon gamma and tumor necrosis factor (TNF). Released cytokines increase inflammation with positive feedback. In addition, the continuous production of nitric oxide and ROS increases the toxic effects of radiation-induced inflammation on healthy tissues. When this response cannot be prevented by anti-inflammatory mechanisms, inflammatory cytokines and free radicals caused by chronic inflammation impair the functions of organs (Azzam et al. 2012; Yahyapour et al. 2018).

Today, the use of radiation in the medical field has become so widespread that it is currently the leading source of artificial radiation across the world. The use of radiation

in medicine accounts for 98% of artificial sources and is globally the second largest source of exposure after natural sources, representing about 20% of all sources. In the world, approximately 23 million people work in environments where radiation sources are used, and about 10 million of these people are exposed to artificial sources. Three of every four workers exposed to artificial sources work in the medical sector, and the annual effective dose per worker is 0.5 mSv (UNEP 2016). The aim of the current study was to reveal the effects of occupational exposure to low-dose long-term ionizing radiation on inflammation and oxidative stress biomarkers in healthcare workers.

Material and Method

Research Design

This study, which was carried out between 4 August and 30 November 2020, was a hospital-based cross-sectional study.

Study Groups

Two groups of participants were formed with people working in departments involving exposure to ionizing radiation (radiology, nuclear medicine, radiation oncology, cardiology, orthopedics, urology, and gastroenterology) and those working in departments without exposure to ionizing radiation (emergency medicine, forensic medicine, family medicine, anatomy, biochemistry, internal medicine, infection, physiology, chest diseases, public health, obstetrics, microbiology, pathology, pediatrics, mental health and diseases, sports medicine, and medical biology).

Research Sample

According to the oxidative stress and inflammation indicators, the minimum sample size for the t-test in independent groups was calculated as 172 healthcare workers, with a power of 90%, medium effect size of 0.5, type 1 error of 5%, and a group ratio of 1:1 using G-power software (Faul et al. 2007, 2009). Of the 199 healthcare workers exposed to IR in the departments of radiology, nuclear medicine, radiation oncology, cardiology, gastroenterology, orthopedics and urology at the hospital, 86 were selected with simple random sampling, weighted according to the departments, from the employee lists obtained from the hospital chief physician and included in the sample using the stratified sampling method. Eighty-six workers with similar characteristics to the IR group (age, gender, smoking, alcohol consumption, presence of chronic diseases, antioxidant supplement use, and exposure to radiation for medical diagnosis and treatment within the last year), who were working in departments that did not involve exposure to IR were included in the sample as the non-IR group. The calculated sample size was reached by conducting the research with 172 participants who agreed to participate in the research.

Data Collection

After informing the participants in detail about the study and obtaining both their verbal and written consent, a data collection form was administered to the participants at the department where they worked. In addition, blood samples were taken into flat-bottom gel and clot activator tubes after at least eight hours of fasting in the morning.

Blood Samples

Blood samples taken under sterile conditions were centrifuged in flat-bottom biochemistry tubes at 1,000 g at room temperature for 10 minutes (HettichRotina 46R refrigerated centrifuge device), and the supernatant serum was transferred to a conical capped microcentrifuge tube and stored at -20 °C. From the samples taken, the serum levels of IL-10 and TNF-α were measured with the enzyme-linked immuno-sorbent assay using the AndyGene commercial kit (AndyGene, China). TAS was measured using the Bioassay commercial kit (BT Lab, China) and TOS was determined using the AndyGene brand commercial kit (AndyGene, China) with the spectrophotometric method (Erel 2004, 2005). The AndyGene and BT Lab kit results for the TAS and TOS serum levels were compared with the RelAssaykits, and the calculations were checked. The oxidative stress indicator (OSI) was obtained by dividing TOS by TAS (Selek 2007).

Institutional Review Board Statement and Funding

After receiving approval from the Non-Pharmaceutical and Medical Device Research Ethics Committee of Necmettin Erbakan University Meram Medical Faculty (Date: 07/02/2020, Number: 2020/2299), the study was conducted at the hospital of university. Necessary written permission was obtained from the chief physician of the medical faculty. The study was funded by the Scientific Research Projects Coordinatorship of Necmettin Erbakan university (project number:

201518006).

Statistical Analyses

The data obtained as a result of the study were transferred to the computer environment and SPSS v. 17.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. In descriptive analyses, categorical data were presented as numbers (n) and percentages (%) while numerical data were summarized using arithmetic mean ± standard deviation. It was accepted that the data were normally distributed according to the central limit theorem (Dawson-Saunders 1990). The chi-square ($\chi 2$) test was used to compare categorical data, and Student's t-test (t-table statistics) was used to compare numerical data. The Pearson correlation test was used to examine the relationship between TOS, TAS and OSI and duration of employment (years) in the IR group. The correlations were interpreted as low or non-significant if the R value was 0.05-0.30, low-moderate if 0.30-0.40, moderate if 0.40-0.60, good if 0.60-0.70, very good if 0.70-0.75, and perfect if 0.75-1.00. The receiver operating characteristics (ROC) analysis was used to examine the sensitivity, specificity and cut-off values of the serum TAS, TOS, OSI, TNF-α, IL-10 biomarkers in predicting oxidative stress and inflammation caused by IR. The statistical significance level in all analyses was accepted as $p<0.05$.

Table 1. Distribution of the characteristics of the study groups

		IR group (n = 86)	Non-IR group (n = 86)		
		n (%)	n (%)	χ^2	p
Gender	**Male**	43 (50.0)	36 (41.9)	1.147	0.284
	Female	43 (50.0)	50 (58.1)		
Smoking status	**Smoker**	30 (34.9)	26 (30.2)	0.424	0.515
	Non-smoker	56 (65.1)	60 (69.8)		
Alcohol use	**Present**	8 (9.3)	4 (04.7)	1.433	0.231
	Absent	78 (90.7)	82 (95.3)		
Chronic disease	**Present**	26 (30.2)	25 (29.1)	0.028	0.867
	Absent	60 (69.8)	61 (70.9)		
Regular medication use	**Present**	22 (25.6)	22 (25.6)	0.000	1.000
	Absent	64 (74.4)	64 (74.4)		
Antioxidant supplement use	**Present**	10 (11.6)	9 (10.5)	0.059	0.808
	Absent	76 (88.4)	77 (89.5)		
Medical radiation exposure	**Present**	35 (40.7)	26 (30.2)	2.058	0.151
	Absent	51 (58.3)	60 (69.8)		
	Mean ± SD (years)	**Mean ± SD (years)**		**t**	**p**
Age	35.91 ± 7.07	34.96 ± 8.25		0.813	0.417
Smoking duration	10.97 ± 5.50*	9.63 ± 6.59**		0.833	0.408
Chronic disease duration	8.71 ± 8.58***	7.36 ± 6.77****		0.622	0.537
Employment duration	9.80 ± 7.18	10.45 ± 8.46		0.546	0.586

IR, ionizing radiation; SD, standard deviation
*Smokers in the IR group were evaluated (n = 30).
**Smokers in the non-IR group were evaluated (n = 26).
***Participants with chronic diseases in the IR group were evaluated (n = 26).
****Participants with chronic diseases in the non-IR group were evaluated (n = 25).

Results

The study was conducted with a total of 172 people, with an equal number of participants being included in the IR and non-IR groups. In the IR group, 50.0% of the participants were men, the mean age was 35.91±7.07 years, and the mean duration of employment was 9.80±7.18 years. In the non-IR group, 41.9% of the participants were men, the mean age was 34.96±8.25 years, and the mean duration of employment was 10.45±8.46 years.

The rate of smokers was 34.9% for the IR group and 30.2% for the non-IR group. Among the smokers, the mean duration of smoking was calculated as 10.97±5.50 and 9.63±6.59 packs/year in the IR and non-IR groups, respectively. When alcohol use was examined, 9.3% of the participants in the IR group stated that they consumed alcohol while 4.7% of those in the non-IR group consumed alcohol.

It was determined that 30.2% of the participants in the IR group and 29.1% of those in the non-IR group had a chronic disease. Among the people with chronic diseases, the mean duration of disease was 8.71±8.58 and 7.36±6.77 years for the IR and non-IR groups, respectively. Regular medication use was present in 25.6% of the participants in each group. Ten participants in the IR group (11.6%) and nine participants in the non-IR group (10.5%) were using antioxidant supplements.

It was observed that 40.7% of the participants in the IR group and 30.2% of those in the non-IR group had been exposed to radiation for medical diagnosis and treatment within the last year. When the participants in the IR and non-IR groups were compared in terms of gender, age, smoking-alcohol use, presence of chronic diseases, regular medication use, antioxidant supplement use, exposure to radiation for medical diagnosis and treatment within the last year, and duration of employment, no statistically significant difference was found ($p>0.05$, **Table 1**).

When the oxidative stress markers were examined, the mean TOS and OSI values were higher in the IR group (7.15±4.34 and 0.68±0.60, respectively) than in the non-IR group (5.24±3.60 and 0.39±0.38, respectively). The mean TAS value was lower in the IR group (1.37±0.40) compared to the non-IR group (1.75±0.50). When the mean TOS, TAS and OSI values were compared between the IR and non-IR groups, there were statistically significant differences ($p=0.002$, $p<0.001$, and $p<0.001$, respectively, **Figure 1**).

In the IR group, there was a negative, low-level and statistically significant relationship between duration of employment and the TOS and OSI values ($r=-0.283$, $p=0.008$ and $r=-0.265$, $p=0.014$, respectively) and a positive, low-level and statistically significant relationship between duration of employment and TAS ($r=0.241$, $p=0.026$).

When the mean TAS, TOS and OSI values of the IR group were compared according to gender, smoking, alcohol use, presence of chronic diseases, regular medication use, antioxidant supplement use, and exposure to radiation for medical diagnosis and treatment within the last year, no statistically significant difference was found ($p>0.05$).

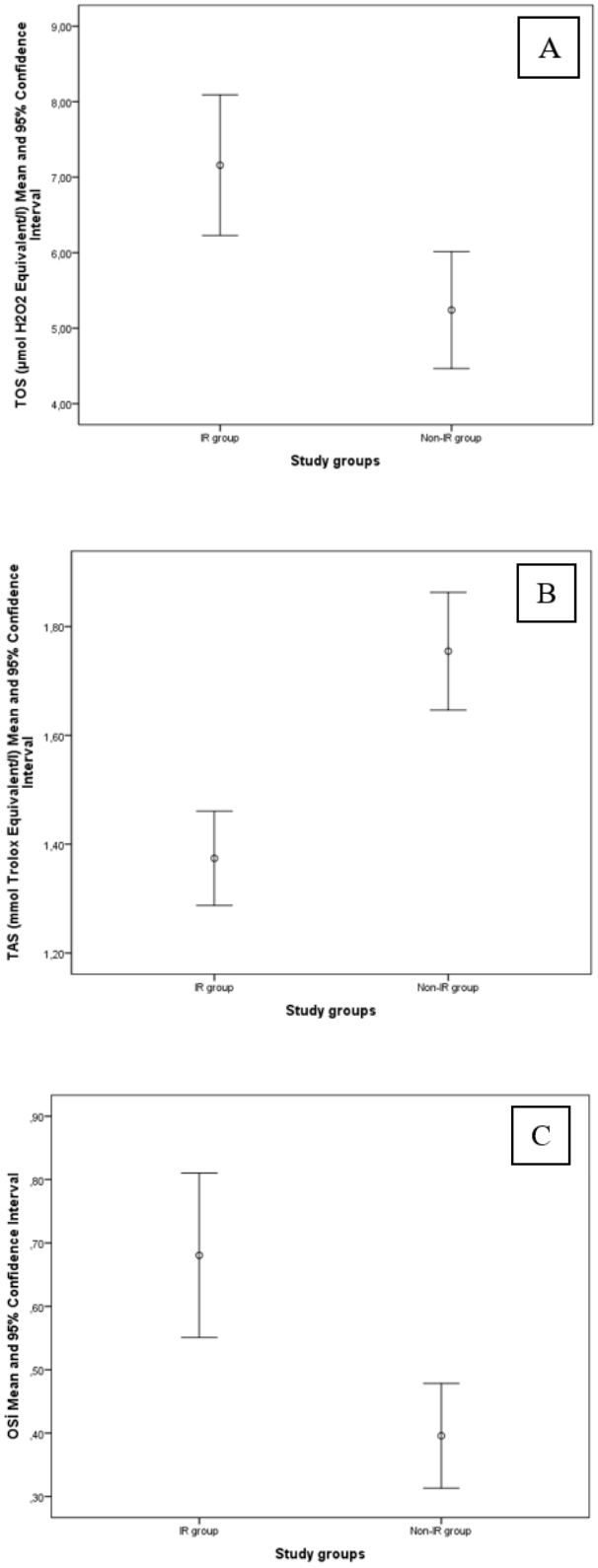
In the ROC analysis, when the cut-off value was taken as 3.47 μmol H_2O_2 Equivalent/l, TOS had a sensitivity of 70.9%, specificity of 53.3%, positive predictive value of 60.4%, and negative predictive value of 64.8% [area under the curve (AUC)=0.655; 95% confidence interval (CI)=0.574-0.736, **Figure 2**). At a cut-off value of 1.6750 mmolTrolox Equivalent/l, TAS had 73.3% sensitivity, 54.7% specificity, 61.8% positive predictive value, and 67.1% negative predictive value (AUC=0.712; 95% CI=0.636-0.788; $p<0.001$, **Figure 3**). For OSI, sensitivity was 70.9%, specificity 58.1%, positive predictive value 62.9%, and negative predictive value 66.7% at the cut-off value of 0.2250 (AUC =0.679; 95% CI=0.599-0.758, **Figure 2**).

When the inflammation biomarkers were evaluated, while the mean TNF-α value was 699.57±243.49 in the IR group, it was 518.31±208.21 in the non-IR group. The mean IL-10 value was 456.19±220.90 and 605.68±301.10 in the IR and non-IR groups, respectively. The mean TNF-α value was significantly higher and the mean IL-10 value was significantly lower in the IR group compared to the non-IR group ($p<0.05$, **Figure 1**).

When the mean TNF-α and IL-10 values of the IR group were compared according to gender, smoking, alcohol use, presence of chronic diseases, regular medication use, antioxidant supplement use, and exposure to radiation for medical diagnosis and treatment within the last year, there was no statistically significant difference ($p > 0.05$).

According to the ROC analysis, at a cut-off value of 536.50 ng/l, TNF-α had a sensitivity of 72.1%, specificity of 54.7%, positive predictive value of 61.4%, and negative predictive value of 66.2% (AUC = 0.717; 95% CI = 0.640-0.793, **Figure 2**). In the IR group, when the cut-off value

was taken as 615.00 ng/l, IL-10 had 69.8% sensitivity, 41.9% specificity, 54.5% positive predictive value, 58.1% negative predictive value (AUC = 0.665; 95% CI = 0.584-0.745, **Figure 3**).



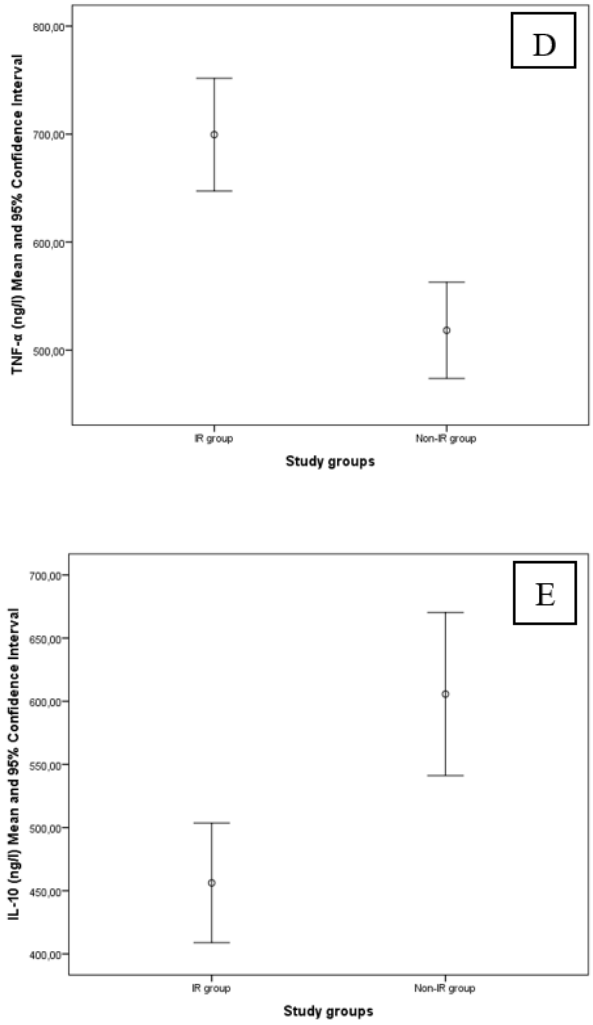


Figure 1. *Oxidative stress and inflammation markers of the study groups. The mean TOS (**A**) and OSI (**C**) values were higher in the IR group (TOS: 7.15±4.34 and OSI: 0.68±0.60) than in the non-IR group (TOS: 5.24±3.60 and OSI: 0.39±0.38) (p=0.002 and p<0.001, respectively). The mean TAS (**B**) value was lower in the IR group (1.37±0.40) compared to the non-IR group (1.75±0.50) (p<0.001). The mean TNF-α (**D**) value was significantly higher and the mean IL-10 (**E**) value was significantly lower in the IR group (TNF-α: 699.57±243.49 and IL-10: 456.19 ±220.90) compared to the non-IR group (TNF-α: 518.31±208.21 and IL-10: 605.68 ±301.10) (p<0.001).*

***IR**, ionizing radiation; **TOS**, total oxidant status; **TAS**, total antioxidant status; **OSI**, oxidative stress index; **TNF**, tumor necrosis factor; **IL**, interleukin.*

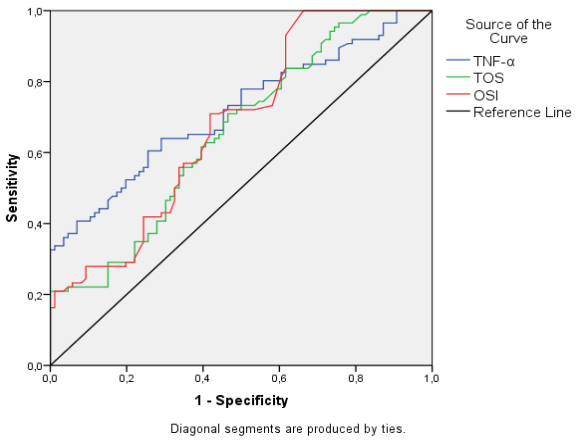


Figure 2. *Receiver operating characteristic curves of tumor necrosis factor (TNF)-α, total oxidant status (TOS) and oxidative stress index (OSI)*

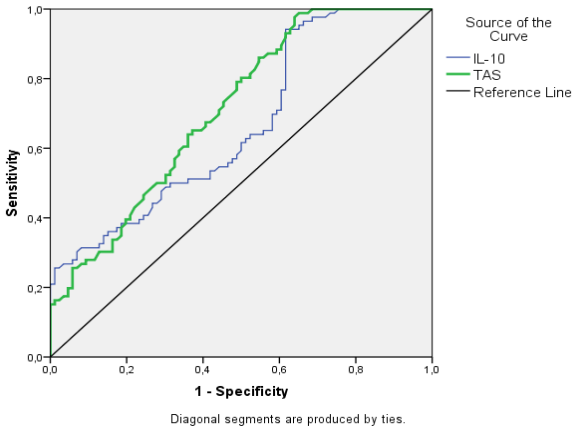


Figure 3. *Receiver operating characteristic curves of interleukin (IL)-10 and total antioxidant status (TAS)*

Discussion

IR has a wide area of use and its effects on human health have been discussed since its discovery. IR sources, which are commonly used in the diagnosis and treatment of diseases, especially in the field of medicine, exert certain effects on healthcare workers due to long-term exposure at low doses. Today, these health-related effects continue to be investigated, and the importance of protecting from IR sources is increasingly emphasized to ensure occupational safety (Fazel and Einstein 2020; UNEP 2016).

IR can indirectly affect cells, thereby triggering the formation of free radicals and increasing oxidative stress (Sebastià et al. 2020). In the current study, which investigated the oxidant and antioxidant status of individuals working in medical departments involving exposure to IR, the TAS and TOS levels were measured, and OSI was calculated. The TOS and OSI values were found to be higher and TAS was lower among the participants in the IR group compared to those that were not exposed to IR in their work environment. Sebastià et al. (2020) reported that antioxidant markers (TAS and extracellular superoxide dismutase activity) decreased and oxidant markers (thiobarbituric acid reactive substance, nitrites, and nitrates) increased in the group exposed to IR, especially in individuals working in the nuclear medicine unit. Similarly, Çelik (2016) found that the TAS levels were lower and the TOS and OSI values were higher among the x-ray technicians who constituted the IR exposure group compared to the control group. In another study conducted with female nurses, El-Benhawy et al. (2020) determined that the TAS values were lower in those that were exposed to radiation compared to the non-radiation group. In contrast, Malekirad et al. (2005) and Kumar et al. (2016) found the TAS value to be higher in radiology unit workers. Katsarska et al. (2016) and Aneva et al. (2019) reported that the TAS value was higher in nuclear power plant workers who were occupationally exposed to gamma radiation compared to the group without radiation exposure. Katsarska et al. (2016) also noted high levels of ROS in lymphocytes in the group exposed to radiation. Kłuciński et al. (2008) concluded that prolonged exposure to low-dose ionizing radiation reduced antioxidant defenses in workers exposed to x-ray. In the literature, various studies evaluating different oxidative stress biomarkers in hospital workers suggest that oxidative stress is high in people working in the field of IR; however, different views have emerged concerning antioxidant systems (Ahmad et al. 2016; Durović et al. 2008; Eken et al. 2012; Gao et al. 2020; Siama et al. 2019). In the current study, which was conducted with Meram Medical Faculty Hospital workers, the dose of IR exposure was not determined by measurement methods, and it was assumed that people working in areas involving the use of IR sources would be exposed to low-dose chronic radiation. It can be stated that antioxidant values change depending on the dose and duration of exposure to radiation. It is considered that as the exposure dose increases, TAS decreases due to the higher consumption of antioxidants while exposure to IR at low doses over a longer time increases TAS through the higher stimulation of antioxidant systems.

IR can cause inflammation by creating an immune response in tissues (Yahyapour et al. 2018). In the current study, the proinflammatory cytokine TNF-α and the anti-

inflammatory cytokine IL-10 were also examined, and it was found that the TNF-α level was higher and the IL-10 level was lower in people working in the radiation field compared to those that were not exposed to IR in the work environment. In a study conducted with female nurses, El-Benhawy et al. (2020) found that TNF-α and other inflammation indicators (C-reactive protein and interferon gamma) were higher in radiation workers compared to the control group. Aneva et al. (2019) reported higher TNF-α levels and lower IL-10 levels in nuclear power plant workers who were occupationally exposed to low-dose gamma radiation than those who did not work in the radiation unit. Zakeri et al. (2010) observed higher IL-2 and lower IL-10 levels among interventional cardiologists compared to the control group. Heidari et al. (2016) found the IL-10 level to be lower in healthcare personnel working in the radiation unit compared to the control group. In another study conducted with radiology technicians and healthy volunteers, Ahmad et al. (2019) reported higher levels of O^{2-}, IL-6, macrophage inflammatory protein-1α, and IL-1α in the group exposed to radiation exposure, but there was no statistically significant difference in relation to the IL-10 and TNF-α levels. Our results are consistent with the literature and suggest that chronic low-dose IR stimulates inflammation.

In this study, when the mean oxidative stress and inflammation biomarkers were compared according to gender, smoking, alcohol use, presence of chronic diseases, regular medication use, antioxidant supplement use, and exposure to radiation for medical diagnosis and treatment within the last year, no statistically significant difference was found in those working in the radiation field. Siama et al. (2019), evaluating radiology technicians, established linear regression models to explain oxidative stress parameters with variables such as age, gender, tobacco chewing, smoking, family history of cancer, duration of employment, and number of patients handled a day and reported that only smoking and number of patients handled a day decreased the catalase enzyme. In a study by Sebastià et al. (2020), linear regression models were established to explain oxidative stress parameters with the variables of age, gender, smoking, high cholesterol, and dietary antioxidant capacity. The authors reported that smoking and dietary antioxidant capacity decreased TAS while oxidative stress varied according to gender. Gao et al. (2020) included exposure to IR, duration of exposure, and exposure dose in their linear regression models and adjusted regression coefficients according to age, gender, smoking status, and alcohol use. They determined that presence of exposure and increased exposure duration and dose increased oxidative stress, and as these variables increased, a higher activity of catalase, an antioxidant enzyme, was observed. Eken et al. (2012) found no relationship as a result of the multiple regression analyses undertaken to investigate the effects of age, gender, smoking status, duration of employment, and exposure dose on oxidative stress parameters in healthcare personnel working in radiation and non-radiation units. In another study, the multiple regression models established to explain the TNF-α, IL-10 and TAS values in nuclear power plant workers who were occupationally exposed to gamma radiation, Aneva et al. (2019) included age, smoking, presence of high blood sugar, high cholesterol, hypertension, and the cumulative absorbed radiation dose and reported that only the last variable made a statistically significant contribution. The cumulative absorbed radiation dose increased TNF-α and TAS and decreased IL-10. Although some studies indicate that smoking does not affect oxidative stress in healthcare workers exposed to radiation (Aneva et al. 2019; Eken et al. 2012), which is similar to our study, it can be considered that our findings concerning the effect of smoking contradict the literature since cigarette smoke is an abundant source of free radicals and aldehydes that cause oxidative stress and damage to the lung and other tissues in vivo. In clinical studies, it has been reported that long-term exposure to cigarette smoke causes systemic lipid peroxidation and depletion of antioxidants, such as vitamins A and C in the plasma and an increase in inflammatory responses, such as C-reactive protein, fibrinogen, and IL-6 (Akköse et al. 2003; Kayan et al. 2009; Mons et al. 2016; Yanbaeva et al. 2007).

In this study, the cut-off values were also determined for oxidative stress and inflammation indicators. These values can be used to reveal exposure to radiation in future research.

Our results showed that long-term exposure to low-dose occupational IR increased oxidative stress and inflammation by creating an oxidant/antioxidant imbalance in healthcare workers. It was determined that the TAS, TOS, OSI, TNF-α and IL-10 levels did not significantly differ according to gender, smoking, alcohol use, presence of chronic diseases, regular medication use, antioxidant supplement use, and exposure to radiation for medical diagnosis and treatment within the last year among the

radiation workers. Considering that increased oxidative stress and inflammation play a role in the mechanisms of various diseases, healthcare workers should be protected from occupational exposure to IR, and necessary precautions should be taken.

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Institutional Review Board Statement: After receiving approval from the Non-Pharmaceutical and Medical Device Research Ethics Committee of Necmettin Erbakan University Meram Medical Faculty (Date: 07/02/2020, Number: 2020/2299), the study was conducted at the hospital of university.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

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