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The Effect of Occupational Radiation on Tumor Markers of Female Radiologists Working in Nuclear Medicine Departments

Abstract

Breast cancer is the most common cancer in women. Considering that the share of radiation exposure to nuclear medicine is about 12%, radiation exposure and the health of these people are very important. We aimed to investigate and respond to the concerns of these radiologists who receive higher doses than other Imaging departments. Given that carcinoembryonic antigen (CEA) and cancer antigen 15-3 (CA15-3) tumor markers respond very well in the early stages of breast cancer, we assessed their effect along with hematological factors to monitor the health of women working in nuclear medicine in Shiraz. 40 women participated in this study. To increase accuracy, the control group was matched with the case group in terms of age, work experience, marital status, number of children, and history of breastfeeding. After completing the consent form, 5 ml of venous blood was taken from each of the volunteers and transferred to the laboratory for testing. No significant difference was observed between the two groups for tumor markers and hematological factors, although the mean frequency of CA15-3 tumor markers in the radiation group (22.50) was slightly higher than the control group (21.85). According to the results obtained from tumor markers, we found no significant difference between the two groups. Even lymphocytes that are among the most sensitive blood cells to radiation did not show sensitivity to radiation in the nuclear medicine departments, indicating the complexity of the effects of ionizing radiation on the body.

Keywords: *Breast cancer, Tumor marker, CA15-3, Carcinoembryonic antigen*

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Introduction

Because of their occupational conditions, hospital radiologists have been exposed to low doses of radiation for a long time, and their biggest concern is related to serious and irreversible complications such as cancer. Since a very small amount of ionizing radiation for a long time increases chromosomal abnormalities [1] and on the other hand, because the effect of low doses of radiation on health is still a controversial issue [2], radiologists' concerns are quite understandable. Given that the share of people exposed to nuclear medicine is about 12% [3], the radiation status and health of nuclear radiologists are very important in terms of radiation protection.

Several studies have reported the incidence of cancer among radiologists. A study on the incidence of cancer in Chinese radiologists showed that the incidence of skin, lung, and breast cancer is correlated with radiation exposure [4]. Moreover, radiologists with more work experience and higher doses were more likely to get breast cancer [5]. Breast cancer in women is the most common type of cancer in the world and is also the leading cause of cancer-related death in women [6]. Tumor markers are biomarkers found in the blood, urine, or tissues of the body that can increase despite one or more cancers. Tumor markers are produced by the tumor or by the host in response to the tumor [7]. Some tumor markers, such as the carcinoembryonic antigen (CEA) glycoprotein, are used to screen for breast, colorectal, lung, and pancreas cancer. Another marker, cancer antigen 15-3 (CA15-3), is commonly used to monitor patients' response to treatment for metastatic breast cancer [7].

On the other hand, several studies have reported that the combination of multiple markers is more useful in diagnosing some cancers [8-12]. The combination of CA 15-3 and CEA increases sensitivity and accuracy in detecting breast cancer [9, 11-14]. A study in Palestine also examined the effects of low-dose radiation using tumor markers in radiologists and showed that CEA tumor marker expression was 57% higher in radiologists, but the difference was not statistically significant [15]. On the other hand, several studies have shown that the mean serum WBCs and monocytes count were lower in radiologists [16], and some researchers found that there was no significant difference in terms of hematological indices between the radiologists and the control group [17]. Therefore, we aimed to evaluate the effects of ionizing radiation using tumor markers and hematological indices in women working in nuclear medicine departments in Shiraz, southern Iran.

Materials and methods

In this case-control study, all available people, including all-female radiologists working in nuclear medicine departments in Shiraz, southern Iran, which included public, private hospitals, and private centers, were invited to participate in this study. The objectives of the study were explained to the participants, and they were assured that they could leave the study at any time, and their consent for participation was obtained. Women who were sick (i.e. had a liver, kidney, or other diseases) or smoked were excluded from the study to increase accuracy. Ultimately, 20 female radiologists working in nuclear medicine departments were enrolled in the case group, and 20 female employees were also considered as the

control group to reduce the effect of intervention factors and increase accuracy. The control group was matched in terms of age, work experience, marital status, and the number of children.

A contract was signed with the Peyvand laboratory to take blood samples from the volunteers, and also, for the participants' ease, the necessary coordination was done with the nurses to take the blood samples at their workplace. 5 ml of venous blood was taken from each volunteer from the antecubital vein and stored in chelate tubes and transferred to the contracting laboratory for testing. Two CEA and CA15-3 tests were performed with ECL(Electrochemiluminescence) method. The serum level of the CEA tumor marker was measured by ARCHITECT kit and ABBOTT i 2000sr device (American) and the serum level of tumor marker CA15-3 was measured by BRM kit (CA15-3) with IMMULITE 2000 xpi (Siemens, Germany). The obtained data were analyzed by SPSS software, version 25. The collected data were analyzed using Kolmogorov-Smirnov statistical tests, one-way analysis of variance (ANOVA), independent *t*-test, and Pearson correlation coefficient.

Results

The mean±SD ages of the women in the case and control group were 35±5.56 and 35±6.35 years, respectively. The mean±SD work experience in radiologists was 5.01±5.5 years (versus 6.5±6.58 years in the control group). None of the radiotherapists involved in the project received overdoses based on dosage film reports. To interpret the results of the data obtained, we used a cut-off of 30 nl/mg for the CA15-3 tumor marker and a cut-off of 5 nl/mg for the CEA tumor marker. The CEA marker was not higher than the cut-off in both groups. CA15-3 tumor marker was higher in seven and three participants in the control and case groups, respectively.

After statistical analysis, CEA tumor markers showed no significant difference between the two groups. After splitting the groups, the mean frequencies of these tumor markers in the cases and controls groups were 1.1 and 1.25 (nl/mg), respectively. There was no statistically significant difference in the CA15-3 tumor marker levels in both groups, but the mean level of this tumor marker was 21.850 in the control group and 22.450 in the case group (Table 1).

Table 1: Comparison of mean tumor marker between the case and control group

Indicator	Control group Mean and standard deviation	Radiation group Mean and standard deviation	p-value
CEA	1.25±0.46	1.100±0.41	**0.35**
CA15-3	21.85±10.8	22.450±7.9	**0.47**

In the radiologists, the mean of monocyte, hemoglobin (HB), white blood cell (WBC) count, and hematocrit (HCT) levels were higher than the control group, but the level of red blood cell (RBC) and platelet (PLT) counts was lower in the case group compared with the control group. The mean lymphocyte count was equal in both groups. But there was no statistical difference between the two groups in any of the hematological indices (Table 2).

Table 2: Comparison of mean hematological indices between the case and control groups

Indicator	Control group Mean and standard deviation	Radiation group Mean and standard deviation	p-value
WBC	6.55±1.73	6.70±1.00	**0.76**
RBC	4.90±0.55	4.50±0.50	**0.28**
PLT	272.50±45.05	270.00±52.38	**0.98**
HB	12.850±1.27	13.40±1.26	**0.07**
HCT	38.65±3.52	40.40±3.73	**0.26**
MONOCYTE	6.0±2.31	6.1±2.53	**0.97**
LYMPHOCYTE	35±8.8	35±9.0	**0.84**

Correlation of hematological indices and tumor markers in the case and controls

Control group

There was a positive correlation between PLT and body mass index (+0.457), and a positive correlation between HB and HCT was (+0.915).

Case Group

There was a negative correlation between HB and body mass index of (-0.478), and also a positive correlation was found between monocytes and the effective five-year dose of radiation (+0.563). A correlation of +0.627 was observed between lymphocytes and blood cells, and a correlation of +0.465 was observed between the work experience of the radiologists and their PLT count. Also, a correlation of +957 was found between the HCT and HB of radiologists. A negative correlation was found between lymphocyte count and effective five-year dose of radiation (+0.479, Table 3).

Table 3: The correlation between monocyte and lymphocyte counts and the effective 5-year dose of radiation in the radiologists

		EFFECTIVE DOSE IN 5 YEARS	Lymphocyte	Monocyte
EFFECTIVE DOSE IN 5 YEARS	Pearson Correlation	1	-.479*	.464*
	Sig. (2-tailed)		.038	.045
	N	20	20	20
Lymphocyte	Pearson Correlation	-.479*	1	-.289
	Sig. (2-tailed)	.038		.229
	N	20	20	20
Monocyte	Pearson Correlation	.464*	-.289	1
	Sig. (2-tailed)	.045	.229	
	N	20	20	20

Discussion

The only study in the world that examined the association of tumor markers and the effect of radiation on radiologists was the study of Muhammad and colleagues [15]. They used CA125, CEA, and CA19.9 tumor markers and found no significant differences between these markers and stated that their increase was within a normal range, which is similar to our study. They also found that the CEA tumor marker alone had increased by approximately 57% in the radiologists. Besides the tumor markers, hematological factors including WBC, RBC, PT, HB, HCT, and lymphocyte and monocyte counts were also used because hematopoietic cells as well as immune cells, including lymphocytes, are the most sensitive cells to radiation exposure, and many studies have confirmed it [16]. Blood cell count is an indicator of ionizing radiation damage to the hematopoietic system. Nonetheless, in this study, there was no statistical significance in any of the indicators and hematological indices.

We found a good correlation between monocytes and the effective five-year dose of radiation. In the case group, because of long exposure to radiation, many free radicals are produced in the body leading to DNA damage and interference with its synthesis. This triggers the reaction of the body's defense system, WBCs, and in particular neutrophils and monocytes as the body's defense barrier. The more chronic the process of exposure to radiation as a xenobiotic agent, the faster the production and increase of monocyte expression. On the other hand, despite the lack of a significant relationship between lymphocytes in the two groups, we observed a decrease in lymphocyte expression in the radiologists, which is consistent with previous studies [18-20].

On the other hand, with the increase in radiologists' work experience, a correlation of +0.465 was observed between the work experience of the radiologists and their PLT count. On the other hand, their HB level decreased. Therefore, with the reduction of iron storage and HB in the radiologists' bodies, PLT counts increased [21, 22]. The results of our study were consistent with another study not showing a significant difference in any hematological factors in radiologists [23]. Other researchers [24]found that the mean WBC and PLT count decreased in radiologists compared with the control group, which was similar to our results. However, the decrease in WBC count was not consistent with our findings. Moreover, they also did not observe a significant difference in any of the hematological indices.

In another study, there was no significant difference in WBC and RBC counts of the radiologists compared with the control group, which was consistent with the results of our study [25]. Mohammad and co-workers [26] examined the effects of radiation on the hematological indices of radiologists and found that the number of irradiated lymphocytes was significantly higher than the control group, which was not consistent with our results. Other indices did not show any significant difference either.

According to the results of the present study and its comparison with the results of other studies, in addition to ionizing radiation, other internal and external parameters also affect blood cells, and therefore many studies have confirmed the effect of radiation on hematological parameters, while others reject it. It can be concluded that the problem of the effects of ionizing radiation on the body can be very complex. WBC count seems to be the only test performed in hospitals to assess the health of radiation which is not very sensitive in diagnosing the effects of radiation exposure in these people because according to the results of this study, even lymphocytes, as the most sensitive blood cells, did not show sensitivity to the amount of radiation around radiologists in nuclear medicine departments. This may be attributed to staff adherence to the principles and regulations of radiation protection or related to adaptive responses [27] over a long period that has resulted in the protective gene cells remaining at high levels in the radiologists' bodies.

The most important strength of this study is its novelty; according to our search, tumor markers have not been widely used to measure the health of radiologists in Iran and even in the world. The limitation of this study was that it was a cross-sectional study, and a causal relationship cannot be deduced from the results.

Conclusion

Although CEA and CA15-3 tumor markers are important indicators in predicting the recurrence of tumors in the early stages and management of patients, we found no significant difference between the two groups. Even lymphocytes which are among the most sensitive blood cells to radiation did not show sensitivity to radiation in the nuclear medicine departments, indicating the complexity of the effects of ionizing radiation on the body. The best thing that radiologists can do is follow the principles and regulations regarding ionizing radiation protection.

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