

Original Article



Examination of Modern Strategies of Instructing Patients for Radiation Protection in the Nuclear Medicine Department

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Article history:

Received: December 5, 2023

Revised: January 1, 2024

Accepted: January 8, 2024

ePublished: February 20, 2024

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Abstract

Background: In every nuclear medicine center, there are places where people are exposed to more radiation than in other areas. To reduce the radiation exposure of employees and patients referring to these centers, it is necessary to observe special precautions to reduce the amount of dose received by different people, especially in the case of women of reproductive age. This study aimed to educate patients and companions to reduce the harmful effects of ionizing radiation.

Methods: In this study, a questionnaire was used as the measurement tool. It contained demographic information and questions related to the evaluation of the quality of education, the level of awareness of patients and their companions, and also their level of satisfaction with the educational facilities of the center. The sample size included 193 patients who had been referred to the Gamma Scan department of Farshchian hospital. The data collected were analyzed using SPSS 19 software. For validity and reliability, the obtained information was analyzed with the help of mean, frequency, and percentage for qualitative variables.

Results: The results of this study showed no significant correlation between knowledge level and gender ($P=0.178$). However, there was a direct relationship between the two variables of knowledge and level of education which is statistically significant ($P=0.001$).

Conclusion: Measurements and statistical studies showed that in the nuclear medicine department of Farshchian Heart Hospital in Hamedan, the level of awareness of patients regarding radiation protection is weak and needs to be improved.

Keywords: Nuclear medicine, Radiation protection, Education, Awareness

Please cite this article as follows: Khosravi H, Kashi F, Bahraman M. Examination of modern strategies of instructing patients for radiation protection in the nuclear medicine department. Avicenna J Care Health Oper Room. 2024; 2(1):36-42. doi:10.34172/ajchor.46

Introduction

Given the increasing spread of new nuclear medicine methods in the diagnosis of various diseases, the informing methods for the protection of patients and personnel have been of special importance (1,2). The use of radioactive substances has been an important tool in the fields of research and diagnosis since about 50 years ago (3). These materials were initially used as the markers of metabolic pathways in physiological and pathological studies, while today they play an important additional role in imaging whose fields of use are included in the specific field of medical science (4). Protecting patients and radiation workers from unnecessary radiation and observing the rule of "Minimum Dose Consideration" will reduce the dose (leakage) to society and, as a result, will ensure the health of society and human generations. The ionization radiations are accompanied by definite and possible effects (1). The definite effects are a function of the dose delivered to the organs and regions of the body that are seen in radiation above the threshold dose, and with increasing

the dose, these effects get more intense (2,3). On the other hand, possible effects of radiation may appear as cancer in patients or genetic disorders in the next generations (2). Moreover, the risk of possible effects increases with the increase in the absorption dose of the patient (3,4). By applying radiation protection for training patients and radiographers, it is possible to prevent the definite effects of radiation interruption and reduce its possible effects (4). Positron emission tomography (PET) is used to produce three-dimensional images of functional processes in the body to detect the extent of disease development and the progress of treatment (5). In nuclear medicine, a three-dimensional image is obtained by attaching radioactive isotopes to the desired substance or organ and using the rays emitted from the tissue which is used in treatment methods. This is particularly relevant in PET, due to the penetrating 511 Kev γ -rays. Dose constraints should thus be set for planning the exposure of individuals. Staff body doses of 1-25 μ Sv/GBq are reported for PET imaging, with the largest component related to the injection (6). Radio-



drugs are few, but most of the treatment methods are done using Tc99. Radio-drugs can be in liquid form such as Tc99 and 123I or in gaseous form such as 133Xe and 18 Kr (7). After the injection, the drug should be left in the body for an appropriate period of time, that is, it should not be left for a short period of time when the metabolic process of the drug is destroyed and the drug is excreted and not for a long time when the absorbed dose of the drug is increased. The time the drug stays in the body depends on its biological half-life and radiological half (6,7). For instance, a survey on ionizing radiation and radiation protection awareness among radiologic technologists at two medical facilities with different specialties and job descriptions illustrated the importance of identifying needed training items and providing effective training and education for both technologists and patients (7). As a result, radiographers play a vital role in the application of protective measures because they are directly responsible for conducting tests, should be aware of the guidelines for reducing the radiation dose caused by various tests, and should have a proper attitude and performance in this field so that they can minimize the risks caused by radiations (8,9). As the main purpose of this study was to assess patients' and their companions' awareness of the harmful effects of ionizing radiation, it is necessary and unavoidable to protect patients against radiation and comply with safety measures.

Materials and Methods

This study was conducted using a questionnaire, following ethical principles in the nuclear medicine department of Farshchian Hospital in 2022. People from different age groups and education levels were evaluated. Among 193 patients referred to the Gamma Scan department of Farshchian medical education center in a certain period of time, 118 people were randomly selected. The method designed by the research team was such that for all patients, there was a break between receiving the drug and performing the scan. The best part of the training was through slides and images that could be shown on TV. These slides were prepared by researchers to increase the awareness level of patients.

The measurement tool was a questionnaire containing demographic information (e.g., age, gender, and educational qualification), questions related to the evaluation of the quality of education for patients and companions, as well as their satisfaction with the department's educational facilities (Table 1). The questionnaire information was generally divided into three groups: The initial part of the studies was before the scan based on background information, demographics, and education level. The second part was related to post-scanning care, and the important group under study was the women who were investigated separately because this group is extremely important in terms of pregnancy and breastfeeding. Moreover, predetermined questions were examined through questions and face-to-face interviews

Table 1. Demographic Information of Patients Referred to the Nuclear Medicine Center of Farshchian Hospital in Hamedan

	Level of Education			Gender		
	Masters and Ph. D	Bachelor	Associate Degree	Diploma and Sub-diploma	Female	Male
9		35	21	128	117	76
		Total=193				

with clients. The data were then collected in an Excel file. Collected data were analyzed using SPSS version 19 software and the student's t-test, and the results were presented using the mean, frequency, and percentage.

Results

As seen in Figure 1, the total number of clients is 193, of which 118 were randomly selected for this study. The number of female clients was about 22%, which was higher than that of males. According to Figure 1a, the education of most of the people referring to this center was diploma or less. As clear in Figure 1b, the majority of clients were informed of the protection methods using indirect methods such as brochures and posters, showing the necessity of using brochures and posters for education.

Figure 2 presents the diagram of the statistical community of women in the reproductive and breast-feeding ages. According to Figure 2a, only about 30% of the mothers were aware of the breastfeeding conditions after the scan. Additionally, according to Figure 2b, about 42% of women were aware of the conditions of pregnancy after the scan. These percentages suggest that this statistical population as an important and influential group should receive a correct and complete education. The accurate description of fertility and breast-feeding risks in certain time intervals after the scan can effectively reduce the risks such as genetic mutations and diseases caused by the possible and definite effects of radiation.

Figure 3 outlines the level of awareness-giving to patients. According to Figure 3a, the level of awareness of the clients regarding the educational facilities of the ward was very low, and about 91% of the clients had little information. Based on Figure 3b, the level of satisfaction with giving information to patients and companions by the staff was about 6%, clearly showing the necessity of retraining and upgrading the scientific and skill levels of the staff. According to Figure 3c, about 74% of patients had little information about the substance used in the scan and the duration of its presence in their body, that this, figure clearly reveals the necessity of informing patients to have a correct understanding of radioactive substances. According to Figure 3d, about 60% of the clients lacked sufficient information about the diet before and after the scan. According to the studies, the diet before the scan should be rich in protein and should contain small amounts of carbohydrates. They also must avoid consuming bloating vegetables such as cabbage, broccoli, and spinach. The hydration of the patient six hours before the scan can help the fast elimination of the radioactive

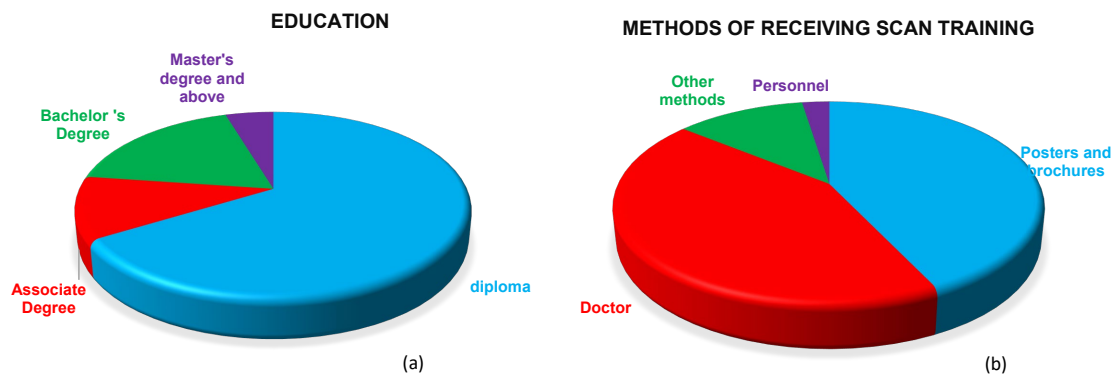


Figure 1. Demographic Information Related to Patients in the PET Scan Department. (a) Education level; (b) Receiving scan training method. *Note.* PET: Positron emission tomography

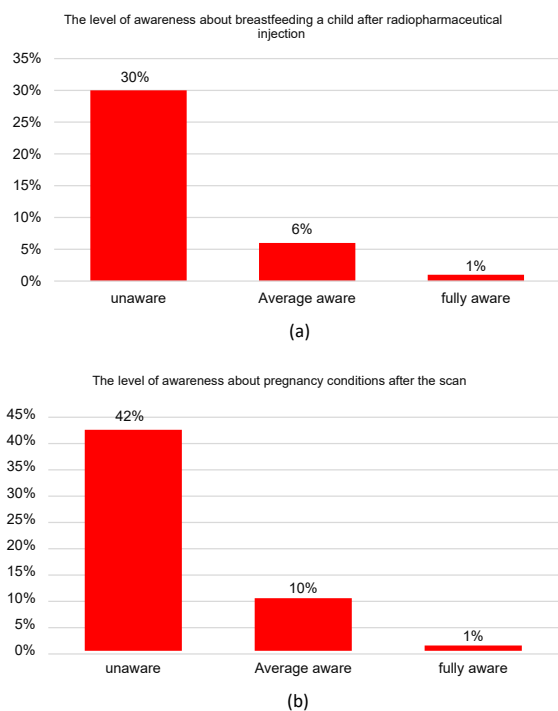


Figure 2. Women of Reproductive Age and Breastfeeding. (a): Level of Awareness of Breastfeeding a Child after Radiopharmaceutical Injection; (b): Level of Awareness of Pregnancy Conditions after Scanning

material by the kidneys (10-26). It should be noted that the above information has been effectively conveyed in the slides prepared by our research team.

Figure 4 shows the amount of care after the scan. According to Figure 4a, the awareness of people about the quarantine (isolation) and the lack of interaction with their surroundings was about 37%, which can expose other family members to radiation. In addition, Figure 4b, indicates that the perception of not using public transportation was considerably at a low level, and only about 36% had an acceptable level of awareness of this issue. An important point in using public transportation is that the clients receiving radioactive substances would use the public transportation system to return to their living place that was usually located far from the imaging center while other passengers and the drivers can be in danger

of receiving radiation. According to the “As Low As Reasonably Achievable” (ALARA) principle, increasing the distance from the patient can effectively reduce the radiation exposure of others. It is recommended that a service be provided for the return of patients by allocating a specific budget. The driver should also apply protection or other protection methods such as keeping a distance from the case, and care should be taken not to be exposed to the risk of radiation. Moreover, Figure 4c illustrates that 60% of subjects had little knowledge about how to dispose of radioactive material from their body. The radiation rate depends on the number of Mille Curie of the source, distance from the source, the linear attenuation coefficient of the material, the thickness of the protective material, and the radiation rate constant of the radio-nucleotides. Moreover, Figure 4d depicts that the majority of the patients lacked sufficient knowledge about returning to work after the scan, and according to the surveys, about 76% of the patients had a low level of awareness of this issue and often considered returning to their jobs as necessary and unobstructed. Therefore, providing educational and informative brochures through secondary message system (SMS) and sometimes to low-educated people and informing by phone can play a significant role in reducing cumulative doses.

Figure 5 shows additional information before and after scanning. Figure 5a indicates the level of awareness of patients about the limitations of CT and magnetic resonance imaging (MRI) after receiving the radioactive substance. According to Figure 5a, it can be said that the level of awareness of patients in this field of examination is extremely low (about 3%). Figure 5b, illustrates the level of awareness of the patients on the presence of prosthetics, batteries, and heart stents in their bodies and the effect of nuclear scanning on these materials. According to this figure, about 96% had little knowledge in this field. Artificial limbs are called technical orthopedics limbs or prosthetics, which are used for treatment or beauty. In general, the presence of a prosthesis did not affect the result of the scan, nor was it destroyed by the nuclear scan. It should also be noted that prostheses, batteries, and cardiac stents have made extensive progress and have

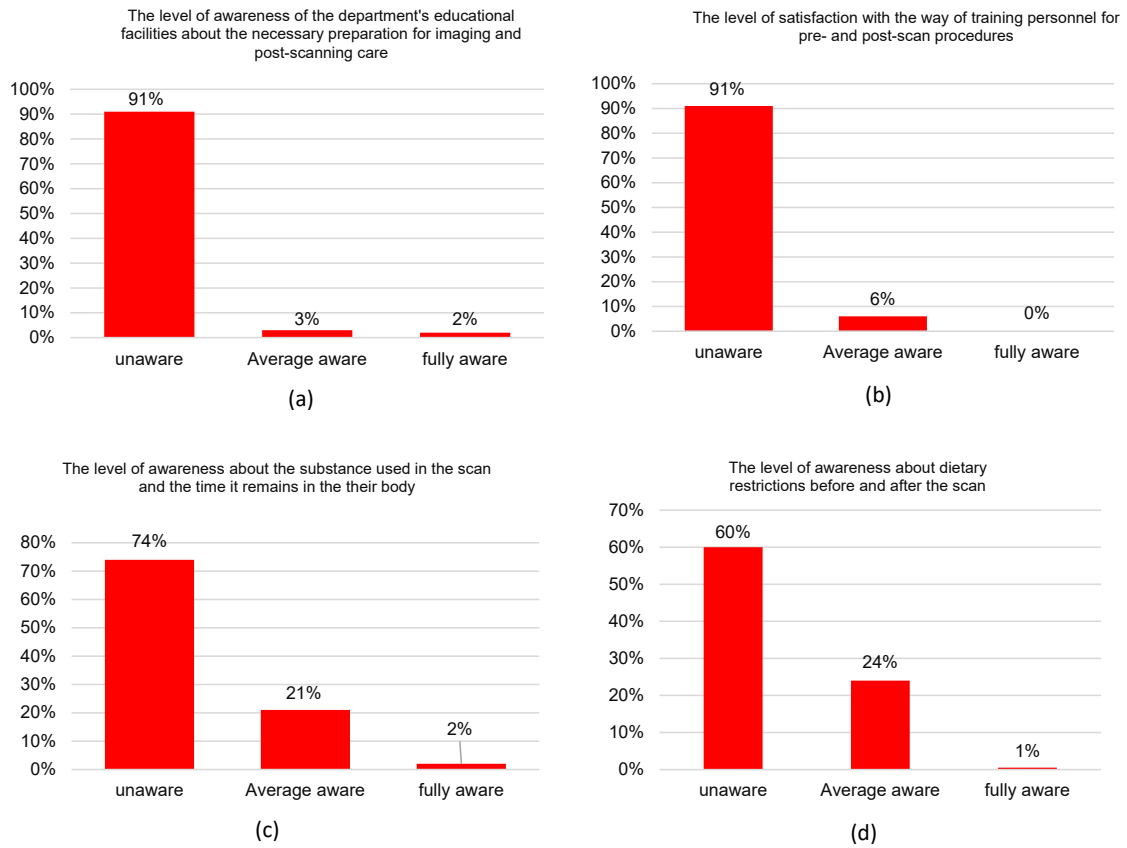


Figure 3. Diagrams Related to How to Inform Patients. (a): Level of clients' awareness of the department's educational facilities regarding the necessary preparation for imaging and post-scanning care; (b): Level of satisfaction with the way personnel are trained for the steps before and after the scan; (c): Awareness of the substance used in the scan and the time it remains in the body; (d): Awareness of food restrictions before and after the scan

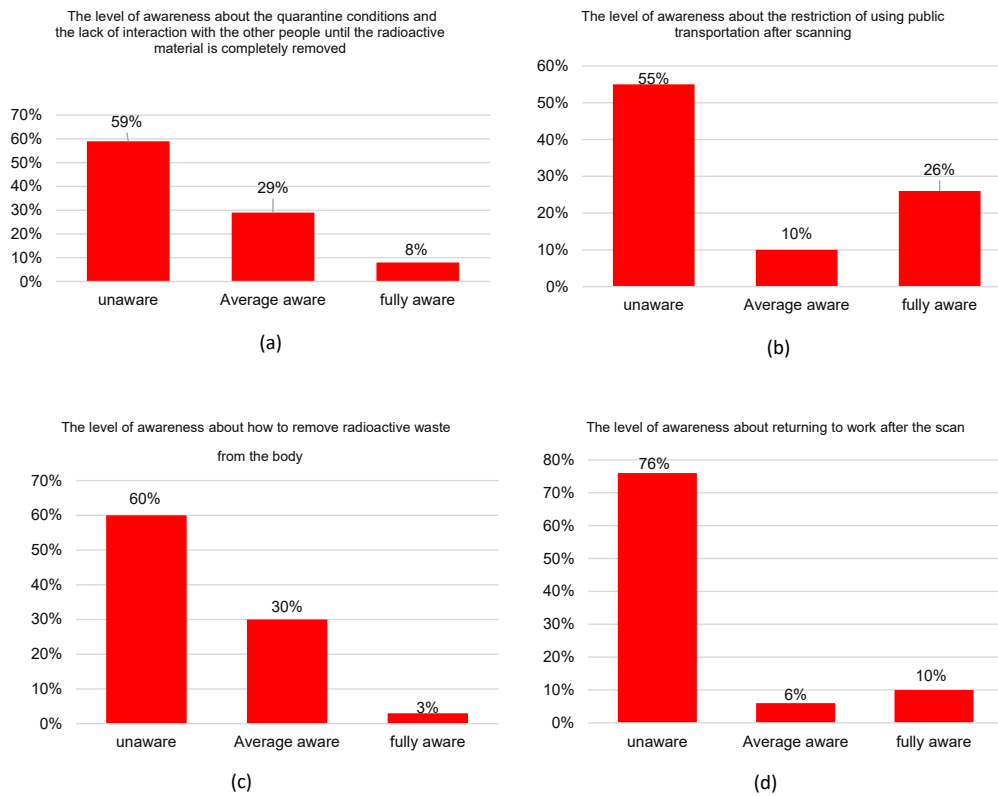


Figure 4. Post-scan Care. (a): Awareness of quarantine conditions and non-interaction with other people until the complete removal of radioactive materials; (b): Awareness of the restriction on using public transport after scanning; (c): Awareness of how to remove radioactive waste from the body; (d): Awareness of returning to work after scanning.

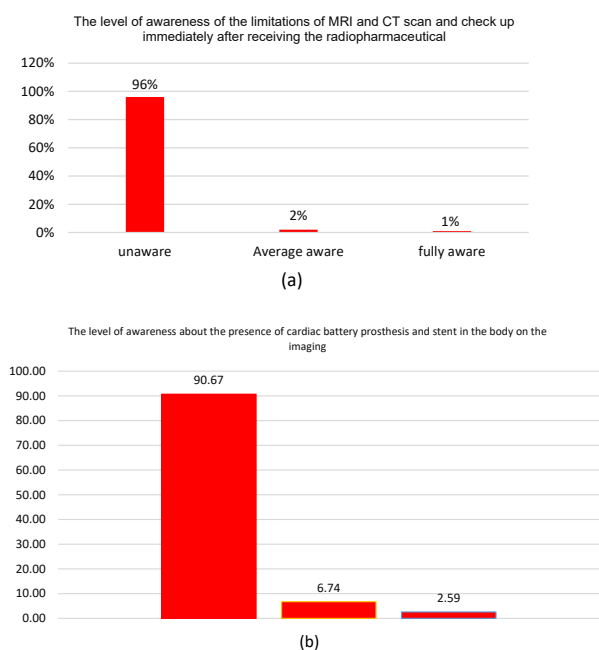


Figure 5. Additional Information after and before Scanning. (a): Awareness of the Limitations of MRI, CT Scan, and Checkup Immediately after Receiving the Radiopharmaceuticals; (b): The level of awareness about the presence of cardiac battery prosthesis and stent in the body on the imaging process.

been adapted to industrial techniques since 1960.

Discussion

The results of this study showed that about 42% of women were aware of the conditions of pregnancy after the scan. These percentages indicate that this group, as an important and influential group, should receive correct and complete training. Accurately explaining the risks of fertility and breastfeeding in specific time intervals after scanning can effectively reduce risks such as genetic mutations and diseases caused by certain and possible effects of radiation. Furthermore, the level of knowledge of clients about educational facilities is extremely low, and 91% of clients had little information. This case clearly reflects the necessity of informing the patient about the correct understanding of the radioactive substance. In addition, 60% of people had little knowledge about how to dispose of radioactive material from their bodies. During the investigations carried out in this study, one of the concerns of the patients was the presence of prosthetics, batteries, and cardiac stents in their bodies and the effect of nuclear scanning on these materials; moreover, about 90% of patients had little knowledge of this issue.

In 2011, a descriptive-analytical study was conducted by Chaparian et al (1) aiming at the assessment of the level of awareness, attitude, and performance of radiologists working in radiology departments of Yazd province. In this study, the measuring instrument was a questionnaire containing 38 questions, which was completed by 112 radiologists working in radiology centers. This questionnaire contained demographic information and questions related to the level of attitude and performance

of radiologists. It was analyzed using SPSS 19 software through non-parametric and Spear-man correlation coefficient tests. The findings indicated a significant and inverse relationship between the age and work experience of radiation workers and their level of awareness. In addition, there was a statistically significant difference in their level of knowledge according to their educational qualifications (degrees). The results of this study revealed that with the increase in the age and work experience and also the decrease in the degree of radiographers, their level of knowledge in this research topic has decreased. To solve this problem, it is better to hold retraining courses containing new protection instructions. Compared with the research conducted on 170 patients, the level of awareness of the patients was evaluated by the research method, similarly with the help of demographic information and the use of SPSS 19 software. Likewise, there was a significant relationship between the level of education of patients and radiographers. Considering the low satisfaction of the patients with the training of the personnel, similarly, there is a need for retraining courses for the personnel of Farchian Heart Center.

In the study conducted by Nordous (11), a pet scan was briefly explained, and the possible risks for pregnant women and young children were investigated. It was reported that pregnant women and women who breastfeed their infants should consider the pet scan as a risk for their infants, every woman should inform her doctor of her pregnancy before performing the scan, and the people who have had a pet scan should avoid pregnant women, infants, and young children in the early hours after doing a pet scan and keep a distance. Similarly, in the conducted study, women of reproductive age and breastfeeding did not have enough information about the required care after receiving the radioactive substance. Moreover, according to the investigation, the patient’s presence in public centers is limited until about 24 hours after receiving the radioactive substance because the patient may expose children and pregnant women to serious risk. As found in this study, patients did not have enough information about this protective method.

Regarding the limitations of computed tomography (CT) and magnetic resonance imaging (MRI), two issues need to be considered: First, the patient performs a nuclear scan and then returns for CT and MRI. In this case, there is no problem in terms of imaging, but the patient attending these centers may be involved or have contact with pregnant women or children under 5 years of age, so it is better to postpone this imaging until 24 hours later when the radioactive substance is completely eliminated from the body. Second, if the patient has a CT scan with oral contrast 24-48 hours before the nuclear scan, 48 hours must pass after the CT scan, but there are no restrictions for MRI. Moreover, some patients referred to the nuclear scan department in the following days can also have blood and urine tests. From a medical point of view, this scan does not affect other tests, but it is better to postpone other

tests for some time later because the radioactive material is still present in the body (blood and urine). Performing such tests should be postponed until after the scan. Over time, it will be removed from the body completely, and the people present in the laboratory, especially pregnant women, children under 5 years old, and laboratory personnel will not be at risk of radiation exposure.

The correlation between the two variables of knowledge and gender was investigated. The rate of correlation was 0.138, indicating a weak correlation between these two variables. In addition, there was a direct relationship between the two variables of awareness and education level with moderate intensity (0.597). This relationship is statistically significant ($P=0.001$), so according to the results, the higher the level of education, the higher the level of knowledge. Based on the obtained results, the correlation rate between these two variables was moderate (0.474). Furthermore, the statistical analyses indicated a negative relationship between the two variables of knowledge and education level with a moderate intensity (-0.495), which is statistically significant ($P=0.001$). Therefore, according to the results, the higher the age of people, the lower the level of knowledge.

Conclusion

According to the studies and the obtained figures, the patients who were referred to the Nuclear Medicine Department of Farshchian Educational and Therapeutic Hospital of Hamedan province did not have enough knowledge about the protective methods before and after the scan. To increase the level of the awareness of the clients we need to improve the level of awareness of the personnel in a useful and scientific way by holding retraining courses taught by university faculty members. New educational methods, including the use of educational slides that can be displayed for patients given the limited information obtained, are of great importance. Therefore, by taking advantage of the department's own facilities and improving the scientific level of the personnel, it is possible to improve the radiation protection of patients. Increasing the awareness of patients can lead to the reduction of the cumulative dose (leakage) of people in society because these people are constantly in contact with family members, and in many cases, they affect other members of society through using public transportation.

Authors' Contribution

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Data curation: Farzaneh Kashi, Maryam Bahraman.

Formal analysis: Hossein Khosravi, Farzaneh Kashi, Maryam Bahraman.

Funding acquisition: Hossein Khosravi, Farzaneh Kashi, Maryam Bahraman.

Investigation: Hossein Khosravi, Farzaneh Kashi, Maryam Bahraman.

Methodology: Hossein Khosravi, Farzaneh Kashi, Maryam Bahraman.

Project administration: Hossein Khosravi.

Resources: Hossein Khosravi, Farzaneh Kashi, Maryam Bahraman.

Software: Farzaneh Kashi, Maryam Bahraman.

Supervision: Hossein Khosravi.

Validation: Hossein Khosravi, Farzaneh Kashi.

Visualization: Hossein Khosravi, Farzaneh Kashi.

Writing-original draft: Hossein Khosravi, Farzaneh Kashi.

Competing Interests

None declared.

Ethical Approval

This study was approved by the Ethics Committee of the Faculty of Paramedic, Hamadan University of Medical Science, Iran (Ethical Code: IR.UMSHA.REC.1400.261). The study participants were informed about the study purpose and answered the questionnaire anonymously; furthermore, they were free to skip any item they did not wish to answer.

Funding

This study is the result of a research project entitled "Examination of Modern Strategies of Instructing Patients for Radiation Protection in the Nuclear Medicine Department" with code number 140004293636, which was conducted in Hamadan University of Medical Sciences.

References

- Chaparian A, Shamsi F, Heydari A. Assessment of awareness, attitude, and practice of radiographers about radiation protection in Yazd province. *Occupational Medicine Quarterly Journal*. 2013;5(1):16-23. [Persian].
- Karami A, Ghaderi S, Moradian S, Mostafae S, Gharibi F, Elahimanesh F. Evaluation of level of knowledge, attitude and performance of radiologists in Sanandaj city regarding radiation protection in 2014. *Scientific Journal of Nursing, Midwifery and Paramedical Faculty*. 2017;2(4):24-32. doi: [10.29252/sjnm.2.4.24](https://doi.org/10.29252/sjnm.2.4.24). [Persian].
- Mirdoraghi M, Fatahi Asl J, Fatahi Asl J. Evaluation of radiation protection condition in educational hospital radiological centers of Ahwaz University of Medical Sciences. *Paramedical Sciences and Military Health*. 2017;11(4):1-8. [Persian].
- Tandon P, Prakash D, Kheruka SC, Bhat NN. Occupational and public exposure to nuclear medicine. In: *Radiation Safety Guide for Nuclear Medicine Professionals*. Singapore: Springer; 2022. p. 59-68. doi: [10.1007/978-981-19-4518-2_6](https://doi.org/10.1007/978-981-19-4518-2_6).
- Tohidniya MR, Amiri F, Khoshgard K, Hormozi Moghadam Z. Evaluation of the observance of radiation protection principles in intensive care units at Imam Reza hospital of Kermanshah. *Payavard Salamat*. 2017;10(6):470-8. [Persian].
- Marengo M, Martin CJ, Rubow S, Sera T, Amador Z, Torres L. Radiation safety and accidental radiation exposures in nuclear medicine. *Semin Nucl Med*. 2022;52(2):94-113. doi: [10.1053/j.semnuclmed.2021.11.006](https://doi.org/10.1053/j.semnuclmed.2021.11.006).
- Yashima S, Chida K. Awareness of medical radiologic technologists of ionizing radiation and radiation protection. *Int J Environ Res Public Health*. 2022;20(1):497. doi: [10.3390/ijerph20010497](https://doi.org/10.3390/ijerph20010497).
- Alipoor R, Mousavian G, Abbasnezhad A, Mousavi SF, Haddadi G. Knowledge, attitude, and performance of radiographers about the principles of radiation protection and following protective standards in medical imaging centers of hospitals in Fasa in 2015. *J Adv Biomed Sci*. 2015;5(4):564-70. [Persian].
- Fakhri AA. Nuclear medicine consultation: a useful tool in primary care to enable more accurate diagnosis. *J Family Med Prim Care*. 2017;6(2):201-3. doi: [10.4103/2249-4863.219997](https://doi.org/10.4103/2249-4863.219997).
- Forsier S. *Essentials of Radiation, Biology and Protection*. 2nd ed. Cengage Learning; 2008.
- What are PET scans, and what are their uses?. <http://www.>

- medicalnewstoday.com/articles/154877.php.
12. Cantone MC, Hoeschen C. *Radiation Physics for Nuclear Medicine*. Springer; 2011.
 13. Anjekika B. Local Radiation Injury. In: Gusev I, Guskova A, Mettler FA, eds. *Medical Management of Radiation Accidents*. Boca Raton, FL: CRC Press; 2001. p. 223-5.
 14. Langford RE. *Introduction to Weapons of Mass Destruction: Radiological, Chemical, and Biological*. John Wiley & Sons; 2004.
 15. Koenig KL, Goans RE, Hatchett RJ, Mettler FA Jr, Schumacher TA, Noji EK, et al. Medical treatment of radiological casualties: current concepts. *Ann Emerg Med*. 2005;45(6):643-52. doi: [10.1016/j.annemergmed.2005.01.020](https://doi.org/10.1016/j.annemergmed.2005.01.020).
 16. Davoudian Talab A, Badiie Nejad A, Beit Abdollah M, Mahmoudi F, Barafraشتهpour M, Akbari G. Assessment of awareness, performance, and attitudes of radiographers toward radiological protective principles in Khuzestan, Iran. *J Health Res Commun*. 2015;1(3):16-24. [Persian].
 17. Karami V, Zabihzadeh M. Review on radiation protection in diagnostic radiology. *Tehran Univ Med J*. 2016;74(7):457-66. [Persian].
 18. Alizadeh M, Khosravanipour MJ, Taghavi M. Evaluating the quantity and quality of radiation protection in Hegmataneh gamma scan nuclear medicine center in Hamadan. *Paramedical Sciences and Military Health*. 2017;12(2):7-12. [Persian].
 19. Movahedi MM, Mehdizadeh A. Evaluation of radiation protection in nuclear medicine department in Namazi hospital according to global accepted standards. *J Fasa Univ Med Sci*. 2013;3(3):224-9. [Persian].
 20. Sadre Momtaz AR, Ghasemi Nezhad SZ. Study of the workers absorbed dose on the basis of their organizational post in three nuclear medicine clinics in Guilan province. *J Guilan Univ Med Sci*. 2012;21(81):53-61. [Persian].
 21. Reagan JT, Slechta AM. Factors related to radiation safety practices in California. *Radiol Technol*. 2010;81(6):538-47.
 22. Behroozi H, Tahmasebi M, Mohebifar B. Evaluation of the prevalence of shielding in patients undergoing conventional radiological procedures (1 work shift-1 X-ray room). *J Patient Saf*. 2018;14(3):133-7. doi: [10.1097/pts.0000000000000180](https://doi.org/10.1097/pts.0000000000000180).
 23. Mojiri M, Moghimbeigi A. Awareness and attitude of radiographers towards radiation protection. *J Paramed Sci*. 2011;2(4):2-5. [Persian].
 24. Marengo M, Martin CJ, Rubow S, Sera T, Amador Z, Torres L. Radiation safety and accidental radiation exposures in nuclear medicine. *Semin Nucl Med*. 2022;52(2):94-113. doi: [10.1053/j.semnuclmed.2021.11.006](https://doi.org/10.1053/j.semnuclmed.2021.11.006).
 25. Linet MS, Applegate KE, McCollough CH, Bailey JE, Bright C, Bushberg JT, et al. A multimedia strategy to integrate introductory broad-based radiation science education in us medical schools. *J Am Coll Radiol*. 2023;20(2):251-64. doi: [10.1016/j.jacr.2022.08.010](https://doi.org/10.1016/j.jacr.2022.08.010).
 26. Adambounou K, Ahonyi KA, Houndetoungan GD, Ouedraogo H, Ntimon B, Sdogas F, et al. Knowledge and perception of nuclear medicine by radiologists in French-speaking sub-Saharan Africa. *Asia Ocean J Nucl Med Biol*. 2022;10(1):68-77. doi: [10.22038/aojnmb.2021.56679.1392](https://doi.org/10.22038/aojnmb.2021.56679.1392).