J Renal Inj Prev. 2021; 10(4): e26.

http://journalrip.com doi: 10.34172/jrip.2021.26

Journal of Renal Injury Prevention

Investigating the consequence of chronic exposure to radiation on renal biomarkers among selected radiologic technologists

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ARTICLE INFO

Article Type:
Original

Article History:
Received: 4 April 2021
Accepted: 25 May 2021
Published online: 31 May 2021

Keywords:
Chronic exposure
Radiation dose
Radiologic technologists
Renal injuries
Renal function tests

ABSTRACT

Introduction: Chronic radiation exposure, particularly among technicians using medical imaging instruments, may contribute to chronic disease, including renal dysfunction. Investigating the potential association of this exposure with biochemical changes may assist disease detection and prevention.

Objectives: The study explores the risk of renal dysfunction among radiologic technologists (RTs) with ten years or more of diagnostic imaging experience to evaluate the association of accumulated radiation doses and possible renal injury.

Patients and Methods: A retrospective analysis was performed on the effective accumulative radiation dose from 2009 to 2019 among RTs of radiological department at a general hospital in southern Saudi Arabia. Blood samples were collected, and key biomarkers analyzed using a fully automated biochemical analyzer. Serum levels of the following were measured; sodium, gamma-glutamyl transferase (GGT), chloride, creatine kinase (CK), calcium, albumin, urea, creatinine, lactate dehydrogenase, total protein and potassium. In statistical analysis, $P < 0.05$ was considered significant.

Results: Even with exposure to only low-level radiation sources, RTs were statistically predisposed to variation in biochemical profiles. RTs exhibited GGT and CK levels higher than that of controls, while serum chloride was significantly low.

Conclusion: The current study found a significant change in renal biochemical profiles among RTs who had worked in a radiological department for more than ten years. The association between GGT, CK with Kidney diseases was reported in several reports. Chronic exposure to radiation may contribute to a rise in GGT and CK levels and reduction of chloride and thus could develop the risk of renal diseases.

Original

Implication for health policy/practice/research/medical education:
In a retrospective analysis among radiologic technologists (RTs) of radiological department at a general hospital in southern Saudi Arabia, we found even with exposure to only low-level radiation sources, RTs were statistically predisposed to variation in biochemical profile.

Please cite this paper as: Makkawi M, Alasmari S, Shubayr N, Alashban Y, Zaman G, Eisa N. Khairy H, Hadi A, Mawkili N. Investigating the consequence of chronic exposure to radiation on renal biomarkers among selected radiologic technologists. J Renal Inj Prev. 2021; 10(4): e26. doi: 10.34172/jrip.2021.26.

Introduction

Cumulative exposure among personnel working with radiation has been linked to several disorders, including skin cancer and leukemia, and is of concern to medical health practitioners (1-3). Early studies showed that the rate of mortality among radiologists was high compared to other medical practitioners (4,5). This rate has declined with the induction of lower occupational exposure to radiation (6). Several reports have demonstrated the effects of radiation on human tissues and organs (7,8), specifically, the use of radiation as a therapeutic method led to hepatic dysfunction or liver cancer for patients

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who had no history of liver disease (9-12). Additionally, an association has been demonstrated between ionizing radiation and renal dysfunction (13). The risk of mortality due to chronic renal disease was reported to be associated with radiation dose regardless of the quantity absorbed dose (6). Additionally, renal radiation therapy is necessary for some cases, but other organs might be affected. Using an appropriate therapeutic dose of radiation may serve to avoid renal damage when radiation is necessary; however, as the kidneys are in the center of the abdomen, protecting them when treating abdominal tumors is difficult (14). Radiation therapy is widely used for treating cancers and showed an impact on kidneys. Radiation nephropathy occurs due to radiotherapy application and the incidence increase when total body irradiation is applied, as for before bone marrow transplantation (7). Besides, nephropathy could occur due to either accident or misuse of nuclear, particularly when absorbed doses are between 5 Gy to 10 Gy (7). Thus, the health effects of chronic occupational exposure in radiologic technologists (RTs) merits further investigation. Kidneys function in filtering waste metabolites and electrolytes from the blood, regulating blood pressure, and balancing fluid levels. The study aims to investigate the function of kidneys for RTs who are exposed daily to varying amounts of radiation.

Objectives

The study aims to examine the risk of renal dysfunction among RTs with ten years or more of diagnostic imaging experience to evaluate the association of accumulated radiation doses and possible renal injury.

Patients and Methods

Study design

The retrospective study was carried out in the department of radiology, Sabya general hospital, Jazan region, Saudi Arabia from August to October 2020. The RTs group consisted of ten RTs who have been working in the radiology field for more than ten years. The participating RTs (five male and five females, aged 30-45 years) were those having the highest thermoluminescent dosimeter (TLD) readings (235.85 to 323.72 uS) among all TLD-measured volunteers. This group was compared to healthy volunteers (n=25) who had no history of radiation exposure.

Radiation dosimetry

All RTs were provided personal bar-coded whole-body TLDs (labeled with the wearer's name, age, and time of use) that were worn at chest level under the lead apron. These TLDs were made of lithium fluoride materials doped with magnesium and titanium (LiF–Mg, Ti), and read using a Harshaw 6600 Plus Automated Reader (Thermo Electron Corporation, Ohio, USA).

This study focuses on the relationship between cumulative radiation dose and relative risk of organ injury. A retrospective analysis was performed on the effective radiation doses experienced by the RTs from 2009–2019. Cumulative radiation dose was calculated using the following equation:

$$D = \sum_{i=1}^{n} X_i$$

Where *D* is the cumulative radiation dose (mSv) and *Xi* is the radiation dose in the i-th year.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. Ethical approval for the study was obtained from the Ethical Committee of Scientific Research, King Khalid University [approval number; (ECM#2020-197) – (HAPO-06-B-001)]. Accordingly, written informed consent was taken from all participants before any intervention. Participants were assured that the information will be used only for research purposes. The data of this retrospective study was extracted from the department of radiology at Sabya general hospital.

Biochemical analysis

Blood samples were collected from all RTs via venipuncture and placed in plain tubes without anticoagulant. Serum was separated from the clot by centrifugation at 3000 rpm for 10 minutes at room temperature. The clear supernatant was immediately transferred to another test tube and used for serum biochemical analysis. Serum levels of sodium (NA), potassium, chloride, calcium, lactate dehydrogenase, gamma-glutamyl transferase (GGT), albumin, total protein, creatine kinase, creatinine and urea were measured using a fully automated biochemical analyzer (DXC 600; Beckman Coulter, California, USA).

Statistical analysis

GraphPad Prism (GraphPad Prism version 9.00 for Mac, GraphPad Software, San Diego CA) was used for statistical analyses. The Mann-Whitney U test was used to compare irradiated participants with non-irradiated controls. *P* values were considered significant when less than 0.05.

Results

The total samples (n = 35) consisted of 25 control participants and 10 RTs, which groups were evaluated for significant differences in median serum biochemical levels. In terms of sodium, there was no significant difference at $\alpha = 0.05$ (Figure 1; controls, M = 138.00 mmol/L, SD = 2.98; RTs, M = 137.83 mmol/L, SD = 1.27; Z-score = 0.33, $P = 0.7385$). For GGT, the control group had a significantly lower median value than the RTs (Figure 2; controls, M = 10.00 IU/L, SD = 9.89; RTs, M = 14.00 IU/L, SD = 4.15; Z-score = 2.31, $P = 0.0206$). Meanwhile, median CL was significantly greater in controls than in RTs (Figure 3; controls, M = 106.00 mmol/L, SD = 2.83; RTs, M = 104.00 mmol/L, SD = 1.96; Z-score = 1.96, $P = 0.0489$). Finally,

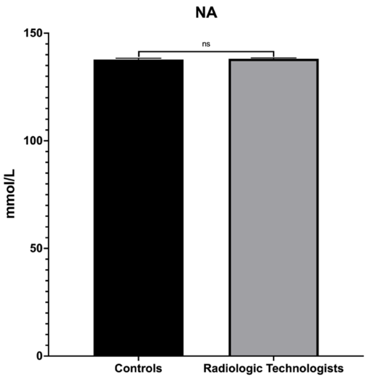

Figure 1. Effect of chronic occupational radiation exposure on serum sodium. The total sample (n = 35) consisted of 25 healthy controls and ten radiologic technologists. Bar indicates median, error line indicates standard deviation.

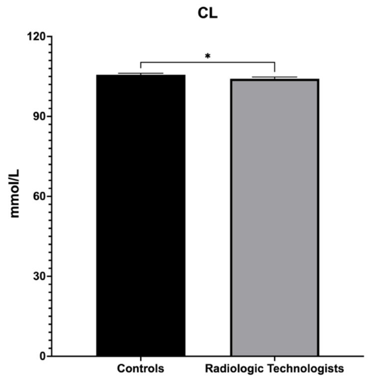

Figure 3. Effect of chronic occupational radiation exposure on serum chloride. The total sample (n = 35) consisted of 25 healthy controls and ten radiologic technologists. Bar indicates median, error line indicates standard deviation.

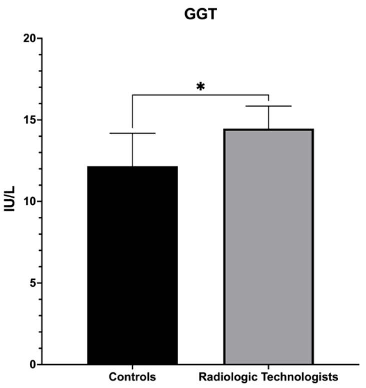

Figure 2. Effect of chronic occupational radiation exposure on serum gamma-glutamyl transferase. The total sample (n = 35) comprised 25 healthy controls and ten radiologic technologists. Bar indicates median, error line indicates standard deviation.

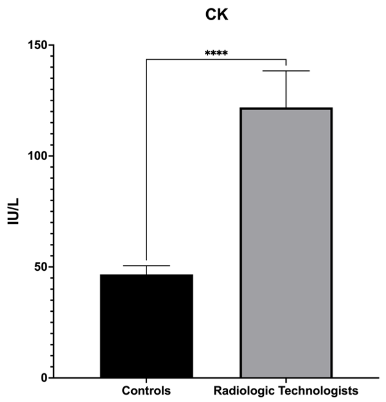

Figure 4. Effect of chronic occupational radiation exposure on serum creatine kinase. The total sample (n = 35) consisted of 25 healthy controls and ten radiologic technologists. Bar indicates median, error line indicates standard deviation.

median CK was significantly lower in controls than in RTs (Figure 4; controls, M = 40.00 IU/L, SD = 19.56; RTs, M = 123.50 IU/L, SD = 49.39; Z-score = 3.89, $P < 0.0001$). No significant differences were observed between the groups for serum calcium, albumin, urea, creatinine, lactate dehydrogenase, total protein or potassium (Table 1).

Discussion

Organs injuries due to ionizing radiation are of concern as an occupational hazard among RTs. Radiation, including but not limited to "irradiation" per se, may affect body organs in several ways. Partial or entire exposures of the human body to doses of radiation as low as 5 Gy in a single fraction are not lethal but may lead to radiation nephropathy, and exposures to even lower doses are associated with late renal disease (15-17). Chronic kidney disease, in particular, is a significant yet underappreciated clinical condition.

Induction of oxidative stress by radiolysis is considered the main consequence of long-term ionizing radiation exposure. This process leads to increased production of free radicals that attack diverse components inside the cell, leading to biochemical changes such as protein oxidation and DNA strand breaks (18,19). Thus, radiolysis and DNA damage may contribute to dramatic changes in biochemical kidney parameters (20), and constant radiation exposure resulting from either treatment or employment may progress to kidney damage. Our investigations evaluate the renal health status of RTs exposed for years to several methods of radiation-based imaging and the possibility of them developing renal injury.

Our findings indicate that chronic exposure of hospital radiation department staff to irradiation may contribute to abnormal changes in renal function. Such chronic exposure is associated with increases in GGT and CK. Clinically, GGT is predominantly tested to assess liver function and used as a diagnostic marker for oxidative stress stimulation and liver disease due to chronic alcohol consumption. However, GGT levels have also been determined to have association with renal dysfunction (21,22) A recent Chinese cohort study likewise revealed a strong relationship between elevation of GGT and the risk

Table 1. Effect of chronic occupational radiation exposure on other serum markers of renal function (n=35)

Test	Median		Z-score (*P* value)
	Control group (n=25)	RT group (n=10)	
Calcium (mmol/L)	2.16	2.08	1.18 (0.2342)
Albumin (g/L)	38.00	39.84	1.12 (0.2613)
Urea (mmol/L)	3.70	3.90	1.64 (0.0995)
Creatinine (µmol/L)	59.50	65.34	0.58 (0.5574)
Lactate dehydrogenase (IU/L)	120.50	143.00	1.28 (0.1988)
Total protein (g/L)	75.00	74.92	0.06 (0.9496)
Potassium (mmol/L)	3.80	3.92	0.67 (0.49880)

RT, Radiologic technologist.

of developing chronic kidney disease (23). This finding was further supported by a more recent Korean study that demonstrated GGT to have potential prognostic use as a risk factor in renal disease, particularly in the end-stage (22). Thus, it is essential to monitor kidney profiles among RTs.

Elevated CK, meanwhile, is considered an indication of rhabdomyolysis (24), and an association has recently been revealed between CK levels in rhabdomyolysis and acute renal failure, with 33%–50% of rhabdomyolysis patients developing acute kidney injury due to the increasing burden of CK (24). Thus, increased CK levels among RTs due to radiation may lead to the possible development of CK-induced kidney disease, further underscoring the need to monitor kidney function in these personnel.

We also identified serum CL levels as significantly attenuated in long-term RTs relative to healthy volunteers. CL plays an important role in the production of hydrochloric acid, acid-base balance, electrical activity, and renal function (25,26). Hypochloremia patients with chronic kidney disease who are still in the pre-dialysis stage have been recently shown to have increased mortality rate and risk of cardiovascular events (27). Interestingly, in the present work, RTs showed reduced serum CL and simultaneous elevation of CK, which is known as an important indicator for cardiac function. These results are consistent with the previous findings in hypochloremia patients (27), and warn of additional risks of chronic radiation exposure. Recently, the association between the use of computed tomography (CT) and electrolytes represents a statistically significant alteration in chloride and sodium (28). In contrast to our study, sodium was dramatically decreased following administration of contrast media. Whereas a reduction in chloride consistent with our observation was seen. All told, results from the current investigation warrant concern regarding the relationship between long-term radiation exposure and variation in key biochemical tests that may indicate renal dysfunction. Therefore, monitoring of renal profiles in radiologic technicians is required to protect these personnel from potential renal disease.

Conclusion

In conclusion, increased risk of renal disease among radiologic practitioners is highly probable due to differences relative to healthy controls in terms of GGT, CK, and CL levels, which biomarkers are directly or indirectly involved in the diagnosis of kidney disease. Establishing routine procedures for monitoring the health status of employees exposed to radiation, even at low doses, is strongly recommended. Such monitoring can be effective in reducing the chance of developing a renal injury. Studying the association between exposure to ionizing radiation and renal disease on such 10 RTs individuals limited our study. However, a larger cohort of RTs with working experience of more than 10 years may strengthen the current observations but hardily achievable.

Limitations of the study

The limitation of this study was latent in recruiting more participants fit for the current research criteria including long work experience at the radiology department. Further studies on a larger participant cohort may improve the knowledge of the association between chronic radiation exposure and health concerns.

Authors' contribution

Conceptualization, MM and SA; methodology, HK, AH and NM; validation, MM and SA; formal analysis, MM and SA; investigation, HK, AH and NM; data curation, NE; writing—original draft preparation, MM, SA, NS, YA and GZ; writing—review and editing, MM, SA, NS, YA and GZ; supervision, MM and SA. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues including plagiarism, double publication, and redundancy have been completely observed by the authors.

Funding/Support
This research received no external funding.

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