G Ital Med Lav Erg 2022; 44:3, 338-346
ISSN 1592-7830

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MEDICINA DEL LAVORO

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Thyroid parameters variations in healthcare workers and students exposed to low-dose ionizing radiations

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ABSTRACT. **Background.** ***Ionizing Radiations (IR) are an important occupational risk factor for the potential damage that can cause to workers' health and for their presence in numerous professional settings. Health care workers (HCW) can be exposed to IR from various sources, in particular from x-rays using radiological equipment, and represent the largest group of workers occupationally at risk, despite increased regulation and protection which caused exposure to low dose radiations. The thyroid gland is one of the most sensitive organs to damage and an important target of IR, leading to functional and organic diseases. The aim of this study is to assess the variations in thyroid hormones, in a population of HCW exposed to low-dose IR.***
Methods. ***121 individuals of the Teaching Hospital Policlinico Umberto I in Rome exposed to low-dose of IR (78 HCW, 17 Residents and 26 Radiology Technicians Students) were observed assessing serum levels of different thyroid function parameters as free triiodothyronine, free thyroxine and thyroid stimulating hormone at T1, T2 and DeltaT. Age, gender, history of thyroid diseases, BMI and smoke were analyzed as possible influencing factors using linear and multiple logistic regression analysis.***
Results. ***Analyzing TSH, fT3 and fT4 serum levels, in two different measurement (T1 and T2) and considering Delta between them, adjusting for different confounding factors, data showed no variation of TSH levels related to occupational exposure, a decrease of fT3 hormone values in HCW and residents, and an increase of fT4 in HCW.***
Discussion. ***The analysis of our results revealed that hospital occupation has an impact on thyroid hormones variations, with an increase of fT4 and a decrease of fT3 and no variations of TSH.***
These results are in conflict with previous studies evidences, in which both free hormones decreased with a concomitant increase of TSH.
Conclusion. ***Exposure to low dose IR influences levels of free thyroid hormones, with no variation in TSH, which could result in a functional or organic disease. For this reason it is recommended continuous surveillance through a periodic check of all the thyroid hormones for an overall view of each HCW. However, further studies are necessary to confirm hormones trend and assess any related thyroid diseases.***

Key words: *TSH, fT3, fT4, healthcare workers, ionizing radiation.*

Background

Radiation in physics is defined as the emission or transmission of energy in the form of waves or particles through space or through a material medium including humans and animal models. Radiation can be classified into ionizing and non-ionizing energy, based on the damaging effect on living tissues (Alawneh, 2018). Ionizing radiation (IR) is a form of energy that causes tissue disorders by removing electrons from atoms and molecules and can travel unseen and pass through materials that include air, water, and living tissue. A familiar example of ionizing radiation is x-rays, which can penetrate our body and alter molecules within the cells of our body (CDC, 2021). Harmful effects of ionizing radiation vary based on dose, exposure time, type of proliferation, and degree of cell differentiation (Luna-Sánchez, 2019).

The thyroid gland is one of the most sensitive human organs to the damaging action caused by ionizing radiations (IR). Usually IR are considered at high doses when exposures higher than 1 Gy occur, whereas for exposures lower than 0.1-0.5 Gy it is deemed at low doses. Adverse effects induced by IR high doses have been extensively studied especially investigating the health consequences of the explosion of the atomic bombs on Hiroshima and Nagasaki, or the Chernobyl nuclear accident. Literature reports an increased incidence of thyroid cancer and nodules, but also a significant growing of thyroid autoimmunity due to high doses of IR and reported the possible role played by IR high doses in the etiopathogenesis of hypothyroidism, Hashimoto disease and Graves hyperthyroidism (Cioffi, 2020). In general the development of thyroid nodules is a common problem and most of them are benign, only 0,3% turn into malignancy and the most frequent form is the papillary or papillary-folliculary adenocarcinoma. The incidence of thyroid cancer had grown from 10 to 100 times due to Chernobyl disaster in high dose IR exposed zones (Epicentro ISS, 2019).

Over recent decades there has been an increased use of IR in medical procedures followed by a significant exposure reduction in general due to more regulation, more workers shifts, use of individual and collective protection devices, but health care workers are still a risk group (Volzke, 2005).

Currently, the attention is focused on the effects on thyroid function and other pathologies related to occupational exposure to low-dose IR, to which health care workers are more easily exposed and considering that IR are an extremely important occupational risk factor (about 30 million workers are professionally exposed to IR) both for the potential damage that can cause to workers' health and for their presence in numerous professional settings like healthcare workers, radiology technicians students and residents.

Most of the available studies have focused on the potential relationship between IR and the development of nodules and malignancy, on the other hand little is known about the possible pathological effects on thyroid function because very few studies investigated hypothyroidism caused by occupational exposure to IR low or very low doses (Alawneh, 2018; Luna-Sánchez, 2019; Chaker, 2017; De Leo, 2016; Antonelli, 1995; De Sio 2016; Caciari, 2014). Furthermore, these studies findings do not allow to extrapolate definite conclusions because of the limited and quite fragmented data.

The aim of our study is to assess the variations in thyroid hormones, such as thyroid stimulating hormone (TSH), free thyroxine (fT4) and free triiodothyronine (fT3), in a population of health care workers, radiology technician students and residents exposed to low-dose of IR, seen in two different medical examinations.

Methods

This retrospective cohort study reviewed data on 121 hospital workers employed in Teaching Hospital Policlinico Umberto I in Rome, Italy who have a history of occupational IR exposure and subdivided into three categories according to hospital occupation.

The category of exposition wasn't considered as a variable but and so to low-dose IR levels. In Italy the ordinance which provides the safety rules relating to protection against ionizing radiations and divides into categories based on the exposure levels is the Legislative Decree 101/2020, hosting the European Atomic Energy Community Directive 2013/59/Euratom, setting the general population limit to 1 mSv.

The employers of Umberto I are subjected to an annual or biannual health examination which includes a complete hematological profile, a physical examination and the evaluation of thyroid hormones, in order to keep a close eye on radiations exposure and for health surveillance in general (according to the Legislative Decree 81/08). Through this medical surveillance all employers data are collected, including socio-demographic data like age, gender and education, anamnestic data like some of the reported in this study, which are:

- Gender;
- Place and date of birth;
- Residential address;
- Name of the agency (Policlinico Umberto I, teaching center in Rome and Sant'Andrea hospital);
- Functional Unit (health care workers, residents and students radiology technicians);
- Years of visits;
- Risk factors (Chemical, physical, biological and night risk and stress);
- Family history for neoplastic, autoimmune and thyroid diseases;
- Weight and height;
- Serum levels of TSH, fT3, fT4 and their variations;
- Previous diagnosis or thyroid diagnosis;
- Any treatment in case of detection of thyroid diseases;
- Smoke;
- Pregnancy.

All of the information collected were reported in a database to be analyzed using SPSS 27.0 statistical program, whereby it was possible to calculate data reported into tables to draw conclusions.

Statistical analysis has allowed the processing of frequency tables as shown. The univariate analysis was carried out using unpaired data Mann-Whitney test and Kruskal-Wallis test for multiple samples. The multivariate analysis included full and backward linear regression models, with dependent variables like TSH, fT3 and fT4; age, gender, role (HCW, residents, students radiology technicians), smoke, BMI and thyroid diseases were independent variables.

The significance level was set on $p < 0.05$.

Results

General characteristics

In Table I the absolute frequency, the percentage and, for age and BMI, the mean and standard deviation of variables of the population assessed are represented. The population consists of a large number of health care workers (78), students radiology technicians (26) and residents (17). The mean age results in 43 years old with a standard deviation of 15,55 years, due to larger sample of health care workers who work for a long time in hospital compared to the residents and student radiology technicians. Regarding the gender instead, females are moderately

Table I. ***Characteristics of the population***

	N (%); Mean (SD)
Age	42,98 (SD 15,55)
Sex	
Male	53 (43,8%)
Female	68 (56,2%)
BMI	20,59 (SD 3,76)
Smoke	
No	90 (74,4%)
Yes	31 (25,6%)
Role	
Students Radiology Technicians	26 (21,5%)
HCW	78 (64,5%)
Residents	17 (14,0%)

more frequent (56,2%); the percentage of smokers is 25,6%, compared to 74,4% of non-smokers; the BMI has shown a mean of 20,59 with a standard deviation of 3,76, describing a healthy population according to dietary habits.

Univariate analysis

Considering all the population, Table II shows a reduction of the median value of TSH between the two measurements (from 2,06 to 1,80) and concurrently a raise of fT4 (from 1,19 to 2,80) and a reduction of fT3 (from 3,30 to 1,36).

Looking at gender results, the hormones follow the same trend, except for TSH, which decreases in women and is stable in men. TSH measurements in T1 and fT3 in T2 are the only ones with a significant association, in fact, women have higher values of thyroid stimulating hormone and lower free-triiodothyronin, in first and second measurement respectively.

There is the same trend of population hormones values for smoke variable. In recent measurements there is an association with smokers lower levels of TSH and fT4 and higher of fT3.

Once again, analyzing roles we have: a decrease of TSH and fT3 and an increase of fT4 in Health Care Workers; this setting is similar in Residents and Students, with the only difference of a decrease of fT4 in the first one and a stable values of fT3 in the second one. Kruskal-Wallis analysis showed an association only in free hormones in both T1 and T2, with higher levels of fT4 in residents and even higher in HCW than Students Radiology Technicians, with a different trend of fT3 which is lower in HCW and higher in Residents.

Finally, focusing on the diagnosis of thyroid disease and comparing values in the two measurements, subjects without any disease have the same thyroid hormones trend of the entire observed population.

After Mann-Whitney analysis significant association has been observed only in free thyroid hormones in both T. In particular, there are mixed results regarding fT4, which is a little higher in T1 and very low in T2 in subjects with diseases, while fT3 had a different behavior, because

Table II. ***Median with Min and Max values for every hormone in the two measurement (T1 and T2) and univariate analysis (Mann-Whitney and Kruskal-Wallis) in each variable considered***

	TSH 1 Median (range)	TSH2 Median (range)	fT4 1 Median (range)	fT4 2 Median (range)	fT3 1 Median (range)	fT3 2 Median (range)
Entire Population	2,06 (0,03-11.28)	1,80 (0,01-11,10)	1,19 (0,67-1,83)	2,80 (0,87-6,20)	3,30 (2,30-5,80)	1,36 0,87-5,13)
Gender						
Males	1,82 (0,14-1,40)	1,80 (0,01-5,10)	1,18 (0,67-1,83)	3,00 (0,87-6,20)	3,40 (2,60-5,40)	1,36 (0,88-5,13)
Females	2,42 (0,03-11,28)	1,81 (0,01-11,10)	1,19 (0,78-1,76)	2,70 (0,90-4,00)	3,28 (2,30-5,80)	1,33 (0,87-4,60)
p	0,012	0,871	0,514	0,347	0,064	0,509
Smoke						
No	2,13 (0,03-11,28)	1,91 (0,01-11,10)	1,22 (0,67-1,83)	2,82 (0,87-4,00)	3,30 (2,30-5,80)	1,31 (0,87-5,13)
Yes	1,97 (0,21-4,92)	1,76 (0,05-5,10)	1,14 (0,78-1,70)	1,71 (0,87-6,20)	3,30 (2,30-5,40)	2,60 (0,90-4,20)
p	0,201	0,088	0,103	0,088	0,562	0,073
Role						
Students Radiology Technicians	2,15 (0,63-11,28)	1,84 (0,01-11,10)	1,03 (0,78-1,54)	1,14 (0,87-1,72)	3,48 (2,72-5,40)	3,45 (2,60-4,60)
HCW	2,05 (0,03-5,10)	1,88 (0,01-8,05)	1,17 (0,67-1,83)	3,10 (1,06-6,20)	3,20 (2,30-4,40)	1,19 (0,87-1,85)
Residents	2,04 (0,21-4,92)	1,48 (0,05-3,36)	1,46 (1,12-1,76)	1,32 (0,90-1,71)	3,90 (2,30-5,80)	3,50 (2,20-4,60)
p	0,932	0,196	<0,001	<0,001	<0,001	<0,001
Thyroid Diagnosis						
No diseases	2,05 (0,03-5,35)	1,83 (0,39-11,10)	1,17 (0,67-1,83)	2,84 (0,87-4,00)	3,29 (2,30-5,40)	1,29 (0,87-4,60)
Thyroid diseases	2,30 (0,05-11,28)	1,41 (0,01-3,36)	1,37 (0,79-1,76)	1,34 (0,95-6,20)	3,69 (2,90-5,80)	3,43 (1,08-5,13)
p	0,936	0,075	0,018	0,044	0,008	<0,001

remained higher in both T in subjects with a diagnosed disease.

In Table III are represented variations of thyroid hormones in correlation with Age and BMI variables, wherein age is the only significant, while BMI is not correlated to thyroid changes. Looking at results with a $p<0,05$, the age increase corresponds to an increase of fT4 only in the recent measurement while there is a decrease of fT3 in both T. So, the older subjects have more thyroxine but less triiodothyronine compared to younger people.

Multivariate analysis

In Table IV it is considered the association between thyroid stimulating hormone and the variables assessed (Age, Gender, BMI, Smoke, HCW, Residents and Thyroid diagnosis) using a regression model which shows only statistically significant variables after the removal of confounding factors, in former and recent measure (labelled as T1 and T2), and Delta between them (T1 – T2).

According to Table IV, there is not a statistically significant variable associated in T1, while in backward analysis the female gender has a positive association (0,193) with a p=0,033, therefore a higher TSH value in first measurement in females and no association neither in full analysis nor in backward one in T2.

Thirdly, focusing on Delta T measures the only significant result is the thyroid diagnosis, both in full and backward analysis, with a beta value of 0,306 (p=0,005) and 0,292 ($p<0,001$) respectively, showing that thyroid diseases are linked to higher values of TSH in former measure and so to a decrease in the recent one.

Finally, the evaluation of R2 shows that we have a low reliability of results in all measurements, with a R2 not exceeding 0,106 (in T1 full analysis).

In Table V has been evaluated the trend of fT4 hormone and its correlation with the same variables assessed in the previous one, in the same measurement times.

In T1 there is a positive correlation between BMI, HCW and residents (with the following values: BMI= 0,201; HCW= 0,318; Residents= 0,610), thus showing higher levels of the hormone consequently to professional exposure and higher BMI score in latest measurement.

In T2, in both analyses, unmodifiable variable like age and female gender has a negative correlation (age= -0,181; female gender= -0,123) while HCW and Thyroid diagnosis has a positive one (HCW= 1,104; Thyroid diagnosis= 0,185), confirming once again higher level of ft4 in this workers and showing that thyroid disease may involve an increase of the hormone.

Thirdly, variables with a significant result in Delta T measure are HCW and thyroid diagnosis, with a negative result in the difference between T1 and T2, which means higher values in recent measures and so an increase of the hormone. On the other hand age and female gender, which show a higher Delta with a decrease of the hormone.

Focusing on professional exposure, HCW have higher levels of fT4 in both measurements and Residents have higher levels only in the first one.

Finally, the R2 values in T2 and Delta T seem to be highly reliable with measures near 1, while in T1 we have low values (0,286 in full and 0,272 in backward).

In Table VI there is a negative correlation in T1 for female gender and age, showing lower levels of fT3 in older people and women. Regarding roles, HCW has a negative correlation in T2 and a positive Delta (beta=0,896), while Residents have a positive correlation in T1 and Delta (beta=0,118). The results show that HCW have lower levels in last measurement and a decrease of fT3, whereas residents have higher levels in T1 and an increase compared to Students Radiology Technicians. In contrast with fT4 analysis, where the trend of the hormone was the same in both categories examined, there is an opposite trend.

Lastly, based on R2 values there is a high reliability in T2 and Delta measures and a low in T1.

The comparative analysis of the last three tables shows some important correlations.

Concerning TSH, the only significant correlation is in Delta measure and only with thyroid diagnosis, clearly demonstrating that the trend of this hormone is influenced exclusively by thyroid diseases.

Regarding the two free thyroid hormones it is clear that, in addition to individual characteristics like age, gender, BMI and the presence of a thyroid diagnosis, roles have an important impact on each hormone, causing, as concerns HCW, higher levels of fT4 and lower of fT3.

According to follow-up variable, the univariate analysis (Appendix, Table VII) showed a significant correlation only with the Delta T, while in a later multivariate analysis in which it has been assessed the follow-up in association with all previous variables there is no more statistical significance, like is shown in Tables VIII, IX and X in Appendix. Therefore, it is not proved any important difference between the results of the regression model with and without the variable of follow-up.

Table III. ***Bivariate analysis using Spearman's Correlation coefficient between the Age and BMI variables and variation of thyroid hormones in T1 and T2 measurements***

	TSH 1	TSH2	fT4 1	fT4 2	fT3 1	fT3 2
Age	-0,093 (p=0,311)	0,028 (p=0,760)	0,046 (p=0,619)	0,611 (p<0,001)	-0,324 (p<0,001)	-0,649 (p<0,001)
BMI	-0,137 (p=0,133)	-0,019 (p=0,836)	0,016 (p=0,863)	0,106 (p=0,249)	0,090 (p=0,325)	0,035 (p=0,700)

Table IV. *TSH regression models with standardized coefficients in former measure (T1), recent measure (T2) and Delta between them (T1 – T2), considering all variables in Full row and only statistically significant variables in Backward row, and the coefficient of determination R^2*

	TSH ß (p)		
	T1	**T2**	**DeltaT**
Age			
Full	-0,175 (p=0,305)	-0,075 (p=0,664)	-0,104 (p=0,545)
Backward			
Female Gender			
Full	0,168 (p=0,134)	0,096 (p=0,397)	0,075 (p=0,504)
Backward	**0,193 (p=0,033)**		
BMI			
Full	-0,053 (p=0,63)	-0,022 (p=0,846)	-0,033 (p=0,769)
Backward			
Smoke			
Full	-0,177 (p=0,061)	-0,170 (p=0,078)	-0,010 (p=0,915)
Backward			
HCW			
Full	-0,022 (p=0,91)	-0,099 (p=0,607)	0,079 (p=0,681)
Backward			
Residents			
Full	-0,217 (p=0,085)	-0,183 (p=0,153)	-0,038 (p=0,764)
Backward			
Thyroid Diagnosis			
Full	0,164 (p=0,131)	-0,136 (p=0,214)	**0,306 (p=0,005)**
Backward			**0,292 (p<0,001)**
R^2			
Full	0,106	0,081	0,100
Backward	0,037	<0,001	0,085

Discussion

The low-dose IR exposition has an impact on the thyroid gland. An overall assessment, focusing only on values frequencies in professional categories considered in this study, shows an increase of fT4 and a decrease of TSH and fT3 in HCW.

There was a significant association only with free hormones in univariate analysis, confirmed by the linear regression which established higher values of fT4 and lower values of fT3 in health care workers compared to students radiology technicians, with no association in the variation of TSH.

The lack of a long observation, the little variations observed in general in thyroid hormones in hospital workers exposed to low-dose IR and the research of a specific disease as main purpose, have resulted in a limited number of studies available about this issue.

For example, in a recent study, Cioffi et al. (Cioffi, 2020) focused, with only one measurement, on assessing alterations of thyroid hormonal status in exposed and non-exposed workers, finding an increase in TSH values and a decrease in fT3 and fT4, establishing a condition of hypothyroidism based on specific cut-off values.

Similarly, the retrospective cohort study performed by Wong et al. (Wong, 2019) tried to correlate the low-dose IR exposure with alterations in thyroid hormones, assessing

Table V. ***fT4 hormone regression models with standardized coefficients in former measure (T1), recent measure (T2) and Delta between them (T1 – T2), considering all variables in Full row and only statistically significant variables in Backward row, and the coefficient of determination R^2***

fT4 ß (p)			
	T1	**T2**	**DeltaT**
Age			
Full	-0,168 (p=0,272)	**-0,200 (p=0,009)**	**0,162 (p=0,043)**
Backward		**-0,181 (p=0,011)**	**0,203 (p=0,008)**
Female Gender			
Full	0,066 (p=0,51)	**-0,104 (p=0,036)**	**0,118 (p=0,025)**
Backward		**-0,123 (p=0,003)**	**0,131 (p=0,002)**
BMI			
Full	**0,251 (p=0,012)**	0,048 (p=0,323)	0,007 (p=0,896)
Backward	**0,201 (p=0,013)**		
Smoke			
Full	-0,068 (p=0,422)	0,027 (p=0,518)	-0,041 (p=0,347)
Backward			
HCW			
Full	**0,443 (p=0,010)**	**1,143 (p<0,001)**	**-1,038 (p<0,001)**
Backward	**0,318 (p<0,001)**	**1,104 (p<0,001)**	**-1,095 (p<0,001)**
Residents			
Full	**0,603 (p<0,001)**	0,056 (p=0,316)	0,076 (p=0,193)
Backward	**0,610 (p<0,001)**		
Thyroid Diagnosis			
Full	0,023 (p=0,808)	**0,166 (p<0,001)**	**-0,160 (p=0,002)**
Backward		**0,185 (p<0,001)**	**-0,135 (p=0,004)**
R^2			
Full	0,286	0,826	0,806
Backward	0,272	0,823	0,801

326 health care workers and showing a critical decrease of fT3 and fT4 hormones, with a concurrent correlated increase of TSH and a condition of overt hypothyroidism.

Furthermore, Luna-Sanchez et al. (Luna-Sanchez, 2019) evaluated thyroid hormones alterations in a small sample of 46 health care workers belonging to category A, assessing an increase of TSH values in 1 and 5 years with no modification in serum levels of fT3 and fT4, and showing a condition of subclinical hypothyroidism.

In another study, Alawneh et al. (Alawneh, 2018) evaluated TSH, fT4 and fT3 levels in 50 exposed health care workers and 50 non-exposed, concluding that alterations in serum concentration levels of thyroid hormones are associated to occupational radiation exposure especially among men, in particular with variations in TSH and fT4 with no modifications in fT3, just as the other cited studies with an increase of TSH and a decrease of fT4.

Compared to all the scientific scene studies, one of our stronger benefits was the presence of two measurements, which gave us the opportunity to assess the trend over years in an exposed population of hospital workers, even after several years in some cases. The two times, T1 and T2, allow us to have a follow-up period, which was a considered variable, even if it was rejected after a linear re-

Table VI. ***fT3 regression models with standardized coefficients in former measure (T1), recent measure (T2) and Delta between them (T1 – T2), considering all variables in Full row and only statistically significant variables in Backward row, and the coefficient of determination R^2***

	fT3 ß (p)		
	T1	**T2**	**DeltaT**
Age			
Full	-0,143 (p=0,357)	-0,032 (p=0,562)	-0,042 (p=0,663)
Backward	**-0,223 (p=0,009)**		
Female Gender			
Full	**-0,246 (p=0,017)**	-0,052 (p=0,155)	-0,077 (p=0,229)
Backward	**-0,243 (p=0,003)**		
BMI			
Full	-0,022 (p=0,83)	-0,001 (p=0,968)	-0,010 (p=0,871)
Backward			
Smoke			
Full	-0,027 (p=0,754)	-0,015 (p=0,622)	0,002 (p=0,966)
Backward			
HCW			
Full	-0,115 (p=0,507)	**-0,902 (p<0,001)**	**0,946 (p<0,001)**
Backward		**-0,948 (p<0,001)**	**0,896 (p<0,001)**
Residents			
Full	**0,305 (p=0,008)**	0,004 (p=0,914)	**0,163 (p=0,024)**
Backward	**0,372 (p<0,0001)**		**0,118 (p=0,051)**
Thyroid Diagnosis			
Full	0,049 (p=0,617)	0,053 (p=0,134)	-0,032 (p=0,598)
Backward			
R^2			
Full	0,264	0,904	0,708
Backward	0,258	0,900	0,702

gression in the multivariate analysis and was not displayed in the backward data. The reason may be a too short follow-up period, involving a longer observation with a specific length, assuming that if it had been longer it could have been significant.

Differently from many others, the assessment of multiple variables in the evaluation of the relationship between IR and HCW was one more highlight of this study. In fact, the appraisal of the population characteristics, age and gender, smoke habits, BMI, roles and a thyroid diagnosis, turned out to be important in a general view, demonstrated in several values obtained.

Some restrictions instead were represented in the exposure of the population, in which have been considered professional categories and not typical IR exposure levels, and thus a variety in the sample without a dose-response relationship, not providing data on radiation exposure dose either.

Even with two measurements it was not possible to get an equal length in every HCW using a retrospective evaluation, but a wide selection based on data available from clinical records.

Although some interesting findings could be emphasized from our study, we did not establish any cut-off value for thyroid diseases, we just defined a variation instead; the study results do not allow us to define the presence or not of pathologies, but to understand that professional category and consequently IR exposure involve an effect on the thyroid gland. The most important and significant values considered in this study were free thyroid hormones, commonly not assessed in hospital workers routine checks, while TSH, which was not statistically relevant, is the most common thyroid data for survey and it is not able to describe much about the real thyroid health condition alone.

Moreover, it is not possible to obtain a diagnosis of hypo- or hyperthyroidism or an underlying disease throughout a population analysis without the assessment of the various combinations of the 3 hormones, which allows to understand if the IR exposed has a variation of the thyroid hormones and to find out the individual effective condition.

Conclusion

In conclusion, this study proposes a higher thyroid function alteration risk in health care workers and in general in a hospital population exposed to low-dose IR, stronger in free hormones rather than TSH, and subsequently the need of a regular and more careful thyroid surveillance. Further studies are necessary to confirm this association, the importance of an evaluation of the whole gland parameters and also the importance of defining how much measurements are needed to get an overall and more specific view. Two measurements or more are critical in order to comprehend how deep is the low-dose IR influence in a specific period and in health care population, to see the possible role of different hospital tasks also in association with time and to detect any disease before their manifestation.

Certainly, further studies with larger number of HCW are required to confirm hormones trend, to demonstrate in a wider spectrum the dose-response relationship and to provide a guideline for more suitable precautions for IR exposure.

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Appendix

Table VII. ***Spearman's Correlation coefficient between the Follow-Up variable and variation of thyroid hormones***

	DeltaTSH	DeltafT3	DeltafT4
Follow-Up	-0,006 (p=0,948)	-0,340 (p<0,001)	0,401 (p<0,001)

The univariate analysis shown in Table III demonstrates a correlation between the health care workers follow-up and the thyroid hormones difference, in which there were a statistically significant correlation with DeltafT3 and DeltafT4; in fact, with an increase of follow-up time there is a reduction of fT3 and an increase of fT4.

Table VIII. ***TSH regression models with standardized coefficients in Delta between recent measure (T1) and former measure (T2), considering all variables previously considered, adding Follow-Up variable, in Full row and only statistically significant variables in Backward row, and the coefficient of determination R^2***

TSH ß (p)		
	DeltaT Full	DeltaT Backward
Age	-0,104 (p=0,545)	
Female Gender	0,075 (p=0,505)	
BMI	0,032 (p=0,776)	
Smoke	-0,010 (p=0,918)	
HCW	0,077 (p=0,689)	
Residents	-0,036 (p=0,778)	
Thyroid Diagnosis	0,305 (p=0,006)	0,292 (p<0,001)
Follow-Up	-0,005 (p=0,958)	
R^2	0,100	0,085

Table IX. ***fT4 regression models with standardized coefficients in Delta between recent measure (T1) and former measure (T2), considering all variables previously considered, adding Follow-Up variable, in Full row and only statistically significant variables in Backward row, and the coefficient of determination R^2***

fT4 ß (p)		
	DeltaT Full	DeltaT Backward
Age	0,167 (p=0,038)	0,203 (p=0,008)
Female Gender	0,114 (p=0,031)	0,131 (p=0,002)
BMI	-0,001 (p=0,983)	
Smoke	-0,044 (p=0,321)	
HCW	-1,028 (p<0,001)	-1,095 (p<0,001)
Residents	0,065 (p=0,276)	
Thyroid Diagnosis	-0,156 (p=0,002)	-0,135 (p=0,004)
Follow-Up	0,043 (p=0,356)	
R^2	0,808	0,801

Table X. ***fT3 regression models with standardized coefficients in Delta between recent measure (T1) and former measure (T2), considering all variables previously considered, adding Follow-Up variable, in Full row and only statistically significant variables in Backward row, and the coefficient of determination R^2***

fT3 ß (p)		
	DeltaT Full	DeltaT Backward
Age	-0,041 (p=0,674)	
Female Gender	-0,078 (p=0,226)	
BMI	-0,012 (p=0,854)	
Smoke	0,002 (p=0,976)	
HCW	0,948 (p<0,001)	0,896 (p<0,001)
Residents	0,160 (p=0,031)	0,118 (p=0,051)
Thyroid Diagnosis	-0,031 (p=0,613)	
Follow-Up	0,011 (p=0,842)	
R^2	0,708	0,702