European Thyroid Journal (2024) **13** e230252
https://doi.org/10.1530/ETJ-23-0252

Received 4 December 2023
Accepted 30 January 2024
Available online 30 January 2024
Version of Record published 7 March 2024

RESEARCH

Serum anti-Müllerian hormone is lower in patients with multiple radioiodine dose for treatment of pediatric thyroid cancer

Marise Codeco de Andrade Barreto[1,2], Natalia Treistman[2], Lara Bessa Campelo Pinheiro Cavalcante[2], Daniel Bulzico[1], Fernanda Accioly de Andrade[1], Rossana Corbo[1], Paulo Alonso Garcia Alves Junior[1,2] and Fernanda Vaisman[1,2]

[1]Department of Oncologic Endocrinology, Instituto Nacional de Câncer – INCA, Rio de Janeiro, RJ, Brazil
[2]Department of Endocrinology, Universidade Federal do Rio de Janeiro – UFRJ, Faculdade de Medicina, Rio de Janeiro, RJ, Brazil

Correspondence should be addressed to F Vaisman: vaismanfe@gmail.com

Abstract

Introduction: Treatment of patients with pediatric differentiated thyroid cancer (DTC) often involves radioiodine (RAI), which is associated with increased risks of short- and long-term adverse outcomes. The impact of RAI treatment on the female reproductive system remains uncertain. Anti-Müllerian hormone (AMH) is a marker of ovarian reserve and is related to fertility.

Objective: The aim was to analyze the association between RAI and serum AMH level in women treated with RAI.

Methods: We evaluated women with pediatric DTC treated with RAI at the age of ≤19 years. Serum AMH was measured.

Results: The study included 47 patients with a mean age of 25.1 years (12.4–50.8) at AMH measurement and follow-up of 11.8 ± 8.4 years. The mean RAI administered was 235 mCi (30–1150). Sixteen (34%) received multiple RAI doses (471 ± 215 mCi). Mean AMH level was 2.49 ng/mL (0.01–7.81); the level was 1.57 ng/mL (0.01–7.81) after multiple RAI doses and 2.99 ng/mL (0.01–6.63) after a single RAI dose ($P = 0.01$). Patients who received a cumulative RAI lower than 200 mCi had higher AMH levels (2.23 ng/mL, 0.39–7.81) than those who received more (1.0 ng/mL, 0.01–6.63; $P = 0.02$). In patients with similar cumulative RAI activities, administration of multiple RAI doses was significantly and independently associated with AMH level lower than the reference range for age (HR: 5.9, 1.55–52.2, $P = 0.014$) after age adjustments.

Conclusion: Levels of AMH were lower after multiple RAI doses, especially after a cumulative RAI dose above 200 mCi. More studies are needed to clarify the impact of RAI on fertility considering its cumulative activity and treatment strategy.

Keywords: anti-Müllerian hormone; radiodiodine; pediatric thyroid cancer

Published by Bioscientifica Ltd.
https://etj.bioscientifica.com
© 2024 the author(s)

This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Downloaded from Bioscientifica.com at 02/08/2025 12:32:54PM
via Open Access. This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.
https://creativecommons.org/licenses/by-nc-nd/4.0/

European Thyroid Journal (2024) **13** e230252
https://doi.org/10.1530/ETJ-23-0252

Introduction

The increasing prevalence and excellent long-term survival rates of differentiated thyroid cancer (DTC) have generated worldwide interest in the reproductive health and risk of infertility among adolescents and young women exposed to treatment with iodine-131 (radioiodine (RAI)). However, controversy exists regarding the gonadotoxic effects of RAI in DTC survivors, which may include menstrual irregularity, miscarriage, premature ovarian failure, impaired fertility, and genetic damage causing congenital malformations (1, 2, 3, 4). Although transient oligospermia and decreased ovarian function have been reported in adults after RAI, infertility appears to be rare in these patients, except after high RAI doses (5). Temporary amenorrhea or oligomenorrhea lasting 4–10 months occurs in 20–27% of menstruating women after RAI therapy for thyroid cancer. Although the studies on this topic have included small sample sizes, the long-term rates of infertility, miscarriage, and fetal malformation do not appear to be increased in women after RAI therapy (6). Only a few studies have assessed the fertility and ovarian reserve of DTC survivors treated during childhood or adolescence (7, 8, 9, 10, 11), and little is known about the impact of RAI considering the different pubertal stages and ovary maturity.

The assessment of the ovarian follicular reserve is a crucial aspect of fertility evaluation in women. A reduced ovarian reserve may decrease the reproductive life span and, in some women, progress to premature ovarian insufficiency. Reduced ovarian reserve may present as a decreased reproductive capacity or reduced oocyte quality and quantity (12).

The anti-Müllerian hormone (AMH) measured in serum is a marker of ovarian reserve in the female sex (13, 14) and correlates directly with the number of growing follicles that decrease with aging (15). Previous studies have shown that AMH may decrease after high RAI activity in premenopausal women (16, 17). However, the risks of damage to the reproductive system and depletion of ovarian reserve caused by RAI in DTC survivors treated during childhood have not been well characterized and require further studies.

Based on these considerations, the aim of this study was to analyze the association between RAI treatment strategies and the extent of reproductive impairment and depletion of ovarian follicular reserve in women treated with RAI for DTC during childhood.

Materials and methods

Institutional review board approvals/waivers

Ethical approval was obtained from the institutional review board on July 7, 2017 (CEP/CAAE number 6659517.8.0000.5257). The study was conducted in accordance with the principles of the Declaration of Helsinki, as revised in 2013. All participants (or their legal guardians) signed an informed consent before inclusion and participated voluntarily and freely in the study.

Protocol

This observational, cross-sectional, retrospective study was conducted at the Endocrinology Service of the Brazilian National Cancer Institute (INCA) and at the Federal University of Rio de Janeiro (UFRJ).

The study included women who, between 1980 and 2023, were diagnosed with DTC at the age of ≤19 years and were followed up for at least 6 months. The rationale for choosing 19 years of age as the cutoff lies on the WHO definition of childhood (between 0 and 10 years of age) and adolescence (from 10 to 19 years). The exclusion criteria were the occurrence of neoplasms other than DTC, RAI therapy after the age of 19 years, and a history of medical treatment or conditions with the potential of decreasing ovarian reserve. We established the age cutoff of 19 years, as this age separates pediatric and adult individuals, according to the World Health Organization (18). The study included data collected from paper and electronic medical records, self-administered questionnaires, and blood tests.

Data collection

Thyroid cancer treatment

The following data related to DTC history were collected: date of diagnosis, age at diagnosis, DTC histology and histological subtype, tumor–node–metastases (TNM) staging, type of surgery, date of first RAI treatment, number of RAI therapies, age at the first RAI therapy, cumulative RAI dose, and date and age at the last endocrinology appointment. The follow-up duration was defined as the time between the date of diagnosis and the date of the last endocrinology appointment. A patient was considered to have received a therapeutic dose of RAI when the administered dose was ≥30 mCi, as routine ablation of pediatric patients is not performed at our center except when microscopic disease is suspected. Of note, treatment of pediatric patients with DTC at our center follows the American Thyroid Association Guidelines, and dosimetry-based treatment is not performed (19).

Anthropometric data

We collected the participants' height and weight and calculated their body mass index (BMI).

Gynecological and obstetric data

The collected information included the participants' age at menarche and menopause, pregnancy, age at first pregnancy, number of pregnancies, number of live births, congenital defects or health issues in the

Downloaded from Bioscientifica.com at 02/08/2025 12:32:54PM
via Open Access. This work is licensed under a Creative Commons
Attribution-NonCommercial-NoDerivatives 4.0 International License.
https://creativecommons.org/licenses/by-nc-nd/4.0/

offspring, abortion, premature birth, date of last menstrual period, reproductive treatment, comorbidities with impact on fertility (endometriosis, gynecological surgery, and polycystic ovarian syndrome (PCOS)), and premature ovarian insufficiency. The patient was considered to be menopausal after 12 consecutive months of amenorrhea in the absence of a pathological or physiological cause for the amenorrhea. Premature ovarian insufficiency was defined as the onset of menopause before the age of 40 years (20).

Hormonal data

Blood samples for AMH measurement were obtained by venipuncture at any time during the menstrual cycle. Serum AMH levels were measured using electrochemiluminescence immunoassay (ECLIA; Elecsys AMH, Roche; detection limit: 0.010 ng/mL (0.071 pmol/L); measuring range: 0.01–23 ng/mL (0.071–164.2 pmol/L)). The reference values for AMH for ages 20–50 years, provided by the manufacturer, were as follows: 20–24 years: 1.66–9.49 ng/mL; 25–29 years: 1.18–9.16 ng/mL; 30–34 years: 0.67–7.55 ng/mL; 35–39 years: 0.78–5.24 ng/mL; 40–44 years: 0.10–2.96 ng/mL; 45–50 years: 0.05–2.06 ng/mL. For women with PCOS, the reference values were 2.41–17.10 ng/mL. For patients younger than 20 years, the reference values were 0.44–7.75 ng/mL for girls aged 12–14.9 years and 0.34–10.39 ng/mL (values in µg/L corresponding to 2.5th and 97.5th percentiles, respectively) for girls aged 15–18.9 years (21).

Statistical analysis

Continuous variables with normal distribution were summarized as means and standard deviations, and those without normal distribution were summarized as medians and ranges. A simple exploratory analysis using a Cox model was performed for the first-year and long-term outcomes, and all the variables emerging as significant were entered into a multiple model to estimate hazard ratios (HRs) and 95% CIs predicting the impact of the studied variables. The resulting HRs and adjusted HRs for each variable were compared to check for differences in magnitudes that could indicate modifying effects and/or confounders. The proportional hazards assumption was verified using Schoenfeld residuals. Kaplan–Meier survival analysis was applied to estimate disease-free survival related to sexual maturity. Differences were considered statistically significant when the *P* values were below 0.05. The analyses were performed using SPSS® for Mac, version 21.0 (IBM Corp.).

Results

In total, 114 women were eligible for the study. Of these, 23 were excluded due to age >19 years at RAI treatment and 7 due to a history of other neoplasms. Of the 84 eligible patients, 47 had serum AMH levels measured between May 2022 and March 2023. In total, 26 patients could not be contacted due to unavailability of contact information (incomplete phone number and address) in their medical records, and 11 refused to participate due to the distance from their homes to the center where blood was collected.

Table 1 shows the general characteristics of the 47 participants with AMH measurements. Among these participants, the absolute AMH values were similar in those treated for the first time before vs after menarche, regardless of the age at treatment. Similarly, no significant differences between these two groups were observed regarding age at menarche ($P = 0.67$), use of contraceptive methods ($P = 0.5$), or cumulative RAI activity above 100 mCi. All 17 pregnancies were spontaneous and the percentages of patients with PCOS were not statistically different among the two groups(multiple or single treatment and pregnant or nonpregnant) However, when we restricted the analysis to patients who received an RAI cumulative activity >200 mCi, we found a significant difference in serum AMH levels between those who received a cumulative activity above vs below 200 mCi ($P = 0.02$) and between those who received single vs multiple doses ($P = 0.012$) (Figs. 1 and 2). Of note, these seemed to be independent factors for altered AMH levels in our cohort.

The cohort was subsequently divided into two groups according to the number of RAI treatments (single vs multiple), regardless of the cumulative RAI activity (Table 2). The group that underwent multiple treatments compared with the one that underwent a single treatment had a longer interval between the last RAI dose and AMH measurement, AMH levels more frequently out of the reference range adjusted for age, lower median absolute AMH levels, and a higher median cumulative RAI activity, but the number of patients who became pregnant at least once was not different between these groups. Of note, all patients who underwent multiple RAI doses received a cumulative RAI activity >200 mCi.

In an analysis restricted to the participants with serum AMH levels out of the reference range for age, we observed a significant decrease in ovarian reserve after multiple vs single RAI treatment ($P = 0.002$) and at cumulative activity > 200 mCi vs below this level, but no difference in median cumulative activity between these groups (Table 3).

In our cohort there was one case of miscarriage, 1 case of early menopause but no reports of birth defects or premature delivery.

Discussion

The results of our study show a decreased level of the ovarian reserve marker AMH among women with a

Downloaded from Bioscientifica.com at 02/08/2025 12:32:54PM
via Open Access. This work is licensed under a Creative Commons
Attribution-NonCommercial-NoDerivatives 4.0 International License.
https://creativecommons.org/licenses/by-nc-nd/4.0/

European Thyroid Journal (2024) **13** e230252
https://doi.org/10.1530/ETJ-23-0252

Table 1 General characteristics of the patients with measurements of serum anti-Müllerian hormone levels.

Characteristics	***n*** (%)	**Mean** ± **S.D.**	**Median** (minimum–maximum)
Age at diagnosis (years)	47 (100)	13.6 ± 3.2	13.8 (4.7–18.3)
Age at data collection (years)	47 (100)	26.1 ± 9.1	25.1 (12.4–50.8)
Follow-up (years)	47 (100)	11.8 ± 8.3	12 (1.1–31.6)
Tumor size (cm)	42 (89.3)	2.65 ± 1.2	2.5 (0.8–5.8)
Multifocality	20 (43.5)	N/A	N/A
Extrathyroidal extension	47 (74.5)	N/A	N/A
Lymph node metastasis	36 (76.6)	N/A	N/A
Distant metastasis	26 (55.3)	N/A	N/A
Age at first RAI treatment (years)	47 (100)	14.2 ± 3.3	14.4 (5.4–18.9)
Cumulative RAI activity (mCi)	47 (100)	250 ± 204	150 (30–1150)
Single RAI administration (mCi)	31 (66)	N/A	
Multiple RAI administrations (mCi)	16 (34)	N/A	
Pregnancy (yes)	17 (36.2)	N/A	
AMH (ng/dL)	47 (100)	2.49 ± 2.0	2.12 (0.01–7.81)
AMH out-of-reference range for age	10 (21)	N/A	
Age at AMH measurement	47 (100)	26.1 ± 9.2	25 (12.4–50.8)
Interval (years) between last RAI and AMH measurement	47 (100)	10.7 ± 7.2	10.5 (0.7–26.2)
Pregnancies (*n* = 17)			
Spontaneous	17 (100)	N/A	N/A
PCOS	10 (21.2)	N/A	N/A

AMH, anti-Müllerian hormone; mCi, millicurie; N/A, not applicable; RAI, radioiodine; PCOS: polycystic ovarian syndrome.

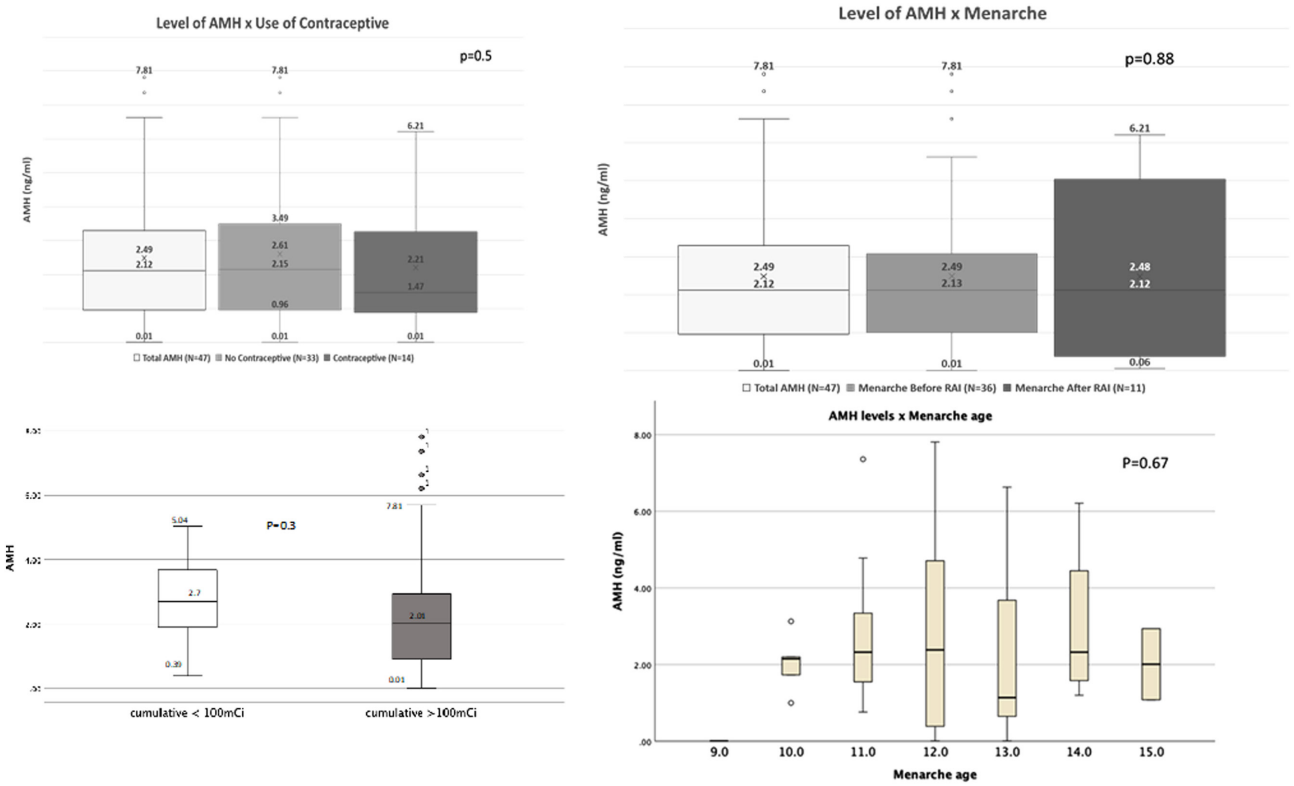

Figure 1

Serum levels of anti-Müllerian hormone related to contraceptive use, menarche before or after radioiodine, age at menarche.

Downloaded from Bioscientifica.com at 02/08/2025 12:32:54PM
via Open Access. This work is licensed under a Creative Commons
Attribution-NonCommercial-NoDerivatives 4.0 International License.
https://creativecommons.org/licenses/by-nc-nd/4.0/

European Thyroid Journal (2024) **13** e230252
https://doi.org/10.1530/ETJ-23-0252

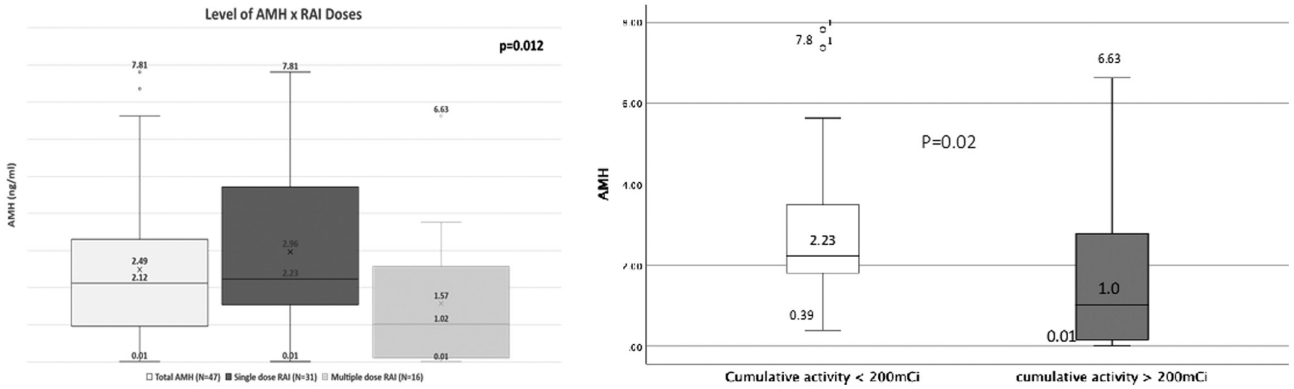

Figure 2

Serum levels of anti-Müllerian hormone associated with multiple doses of radioiodine and cumulative activity of radioiodine above or below 200 mCi.

history of DTC who received RAI treatment during childhood or adolescence in different treatment regiments and also cumulative activity. Patients who received multiple RAI treatments (vs those who received a single RAI dose) and, in particular, those who received a cumulative RAI activity above 200 mCi (vs those who received less than that) were more likely to have lower serum AMH levels, independent of the age in which RAI was administered or pubertal status at treatment. Within the groups, AMH was more frequently out of the reference age when adjusted for age. Interestingly, the median time between the last RAI treatment and AMH measurement was more than 10 years, and AMH level appears to have remained lower even after this long period of time. The cumulative RAI activity was not different between the groups with AMH levels inside or outside the reference range.

Other authors have also shown an impact of RAI on AMH levels, particularly in young adults. Yaish *et al.* have shown that RAI could exert a direct effect on the ovarian reserve, assessed by AMH levels, and reported that patients treated with higher RAI have a significant decrease in AMH concentration. The same has been shown by Evranos *et al.*, who also demonstrated that AMH level decreases shortly after RAI treatment and plateaus at a level lower than the one measured before RAI (17). This would explain our finding of lower AMH levels and higher proportions of AMH levels out of the reference range when more than 10 years had passed since RAI treatment. As shown by van Velsen *et al.* (22), a single RAI treatment significantly reduced the AMH concentration during the first year and remained stable thereafter, although further decline was seen in patients receiving multiple RAI treatments.

Table 2 Characteristics according to radioiodine treatment regimen.

	Entire cohort	Single treatment	Multiple treatments	*P*
n	47	31	16	
Interval (years) between last RAI dose and AMH measurement				**0.03**
Mean ± S.D.	10.7 ± 7.2	9.1 ± 7.1	13.8 ± 6.4	
Median (minimum–maximum)	10.5 (0.7–26.2)	9.2 (0.7–26.2)	14.9 (0.9–24.9)	
AMH out of reference range	10	3	7	**0.002**
AMH measurement range (ng/mL)				**0.012**
Mean ± S.D.	2.49 ± 2.0	2.96 ± 1.7	1.57 ± 0.6	
Median (minimum–maximum)	2.12 (0.01–7.81)	(0.01–7.81)	(0.01–6.63)	
Age at AMH measurement (years)				0.09
Mean ± S.D.	26.1 ± 9.2	28 ± 7.5	31.8 ± 9.4	
Median (minimum–maximum)	25 (12.4–50.8)	25 (12.8–43.5)	31 (12.4–50.8)	
Cumulative RAI activity				**0.001**
Mean ± S.D.	250 ± 204	136 ± 38	471 ± 215	
Median (minimum–maximum)	150 (30–1150)	(30–200)	(250–1150)	
Cumulative RAI activity >200 mCi	20	4	16	<**0.01**
PCOS	10	5	5	0.6
Pregnancy	17	8	9	0.08

Values in bold indicate statistical significance.

AMH, anti-Müllerian hormone; HR, hazard ratio; RAI, radioiodine; PCOS: polycystic ovarian syndrome.

Downloaded from Bioscientifica.com at 02/08/2025 12:32:54PM
via Open Access. This work is licensed under a Creative Commons
Attribution-NonCommercial-NoDerivatives 4.0 International License.
https://creativecommons.org/licenses/by-nc-nd/4.0/

European Thyroid Journal (2024) **13** e230252
https://doi.org/10.1530/ETJ-23-0252

Table 3 Anti-Müllerian hormone levels and radioiodine treatment.

	AMH < RR	**AMH within RR**	***P***	**HR** (95% CI)	***P***
n	10	37			
Interval (years) between last RAI dose and AMH measurement			0.39		
Mean ± S.D.	11.1 ± 7.1	10.5 ± 7.3			
Median (minimum–maximum)	0.9–20.5	0.7–26.2			
Multiple treatments	7 (70%)	9 (24.3%)	**0.01**	5.9 (1.55–52.2)	**0.014**
Use of birth control pills	4 (40%)	16 (43%)	**0.8**		
Age at AMH measurement (years)			0.36		
Mean ± S.D.	26.8 ± 10.6	25.9 ± 8.8			
Range	12.4–44.4	13.2–50.8			
Cumulative RAI activity			0.77		
Mean ± S.D.	360 ± 295	221 ± 165			
Range	100–1150	30–700			
Cumulative RAI activity					
> 200 mCi	8 (80%)	12 (32.4%)	**0.01**	4.16 (0.9–60.92)	**0.09**
>150 mCi	10 (100%)	27 (73%)	**0.2**	1.11 (0.089–13.84)	**0.9**
>100 mCi	9 (90%)	29 (79%)	0.66		
Pregnancy	3 (30%)	14 (37.8%)	0.72		
Follow-up duration (years)			0.43		
Mean ± S.D.	14.4 ± 8.6	11.3 ± 8			
Range	2.9–27.6	1.1–31.6			

Values in bold indicate statistical significance.
AMH, anti-Müllerian hormone; HR, hazard ratio; mCi, millicurie; RAI, radioiodine; RR, reference range.

A meta-analysis published recently by Piek *et al.* (23) showed a significant decrease in AMH levels after RAI therapy. Our study confirms and expands these previous findings of low serum AMH levels in DTC survivors treated with multiple RAI doses during childhood and adolescence. Our evaluation of AMH levels using absolute values in addition to values adjusted by age in a pediatric group was crucial to confirm this effect of RAI, as it is known that AMH typically decreases with age in young women (15).

Studies in patients treated with RAI before the age of 20 years (7, 8, 9) have shown no impact of RAI on fertility, miscarriage, prematurity, or major congenital anomalies. However, these studies included small cohorts and did not evaluate the ovarian reserve. In a Dutch study similar to ours, Nies *et al.* found that female DTC survivors who received RAI treatment during childhood did not appear to have major abnormalities in reproductive characteristics or predictors of ovarian failure (10). The authors observed no differences in AMH levels between women who were DTC survivors and a control group of 420 women not treated for cancer and retrieved from a database. In our study, most AMH levels were not abnormal, except in participants who underwent multiple RAI treatments, which was not analyzed separately in the study by Nies *et al.* In contrast to the Dutch study, the morbidity level of the patients in the present study seems to have been more advanced, as 45% of all patients had distant metastases, as opposed to only 10.7% in that study. This could explain the apparent higher cumulative RAI dose administered to the patients in the present study (i.e. a mean of 250 mCi, increasing up to 1150 mCi in patients who received repeated treatments). In the Dutch study, the median RAI dose was 200 mCi (the 75th percentile was 350 mCi). Indeed, this could explain the more concerning results found in the present study. Therefore, the finding that AMH level is lower in women who received multiple treatments and a cumulative dose above 200 mCi, not found in the less aggressive cases studied by Nies *et al.* (10), could be due to the more aggressive disease in our cohort and a larger number of children undergoing higher cumulative activities and number of treatments.

Aligned with previous studies (10, 16, 17), we found no relationship between the cumulative RAI dose and AMH level, despite the decrease in serum AMH levels observed after treatment. However, we found that the decrease in AMH levels was more evident above the dose of 200 mCi. Unlike the study by Nies *et al.*, we found that multiple RAI doses influenced AMH measurements.

Issues concerning the effect of treatment regimens (single vs multiple doses) and cumulative activity on safety and efficacy remain controversial. Some cases including very young children have shown that for patients treated with 'nontoxic' cumulative RAI activity below 2 Gy, the administration of a single RAI dose was safe, but multiple RAI doses were associated with sequential increases in the overall frequency of cells carrying chromosome aberrations; this occurred mainly due to the induction of unstable chromosome

Downloaded from Bioscientifica.com at 02/08/2025 12:32:54PM
via Open Access. This work is licensed under a Creative Commons
Attribution-NonCommercial-NoDerivatives 4.0 International License.
https://creativecommons.org/licenses/by-nc-nd/4.0/

aberrations, while the proportion of cells with stable chromosome aberrations remained mostly unchanged (24).

Aligned with most literature on this topic, we found no direct influence of RAI on pregnancy. Like the others, our study had a retrospective design and collected data on the occurrence or not of pregnancy. Also, a previous study comparing DTC adult patients treated with surgery and surgery followed by RAI showed similar AMH levels in both groups (25). However, information regarding the time elapsed between the decision to become pregnant and the pregnancy itself, along with other factors that could show increased difficulty in conceiving, could have been missed in all studies (15, 22, 23), including ours. Furthermore, most of our patients were of childbearing age at data collection and may become pregnant in the future with more or less difficulty. Another limitation of the present study is the absence of serum AMH levels measured before RAI treatment; without this information we are unable to know the pretreatment ovarian reserve of our patients. An additional limitation was the fact that the reference range for AMH was provided by the manufacturer, when, ideally, a reference range from a control population would be preferable. However, the reference range for AMH in the present study has been used in previous studies in the Brazilian population and has been shown to correlate well with ovarian reserve (26). Furthermore, besides the relatively small sample (only 47 patients), DTC in children is a rare disease, and our follow-up of a median of more than 11 years strengthens our results. They were all followed up at the same center, had a particularly aggressive disease (as our incidence of metastatic disease is higher compared with other studies), and were followed up by the same medical team, and we were very careful to select patients treated with RAI under 19 years of age, which makes our study different from others that included children and young adults mixed together. It is also worth mentioning that potential confounders of AMH such as PCOS, use of birth control pills, and BMI were not different among the groups. However, PCOS, in particular, is associated with higher levels of AMH and the number of PCOS patients was similar in both groups.

Conclusion

The results of the present study indicate that serum AMH levels are lower in women with a history of DTC who received multiple RAI doses during childhood compared with those who received a single RAI dose, particularly in patients who received cumulative doses above 200 mCi compared with those who received a lower dose than that. This finding should be considered during decisions about RAI activity and regimen and may favor individual dosimetry in patients with metastatic disease in order to accomplish treatment in a single dose. Prospective designed studies could be useful to access more specific data regarding difficulties and time until pregnancy along with pregnancy rates and also how slightly low levels of AMH can impact on pregnancy rates.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the study reported.

Funding

This work did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

References

1 Moon S, Yi KH & Park YJ. Risk of adverse pregnancy outcomes in young women with thyroid cancer: a systematic review and meta-analysis. *Cancers* 2022 **14** 2382. (https://doi.org/10.3390/cancers14102382)

2 Navarro P, Rocher S, Miró-Martínez P & Oltra-Crespo S. Radioactive iodine and female fertility. *Scientific Reports* 2022 **12** 3704. (https://doi.org/10.1038/s41598-022-07592-8)

3 Adamska A, Tomczuk-Bobik P, Popławska-Kita AB, Siewko K, Buczyńska A, Szumowski P, Żukowski Ł, Myśliwiec J, Zbucka-Krętowska M, Adamski M, *et al.* Assessment of different markers of ovarian reserve in women with papillary thyroid cancer treated with radioactive iodine. *Endocrine Connections* 2021 **10** 1283–1290. (https://doi.org/10.1530/EC-21-0187)

4 Anderson C, Engel SM, Weaver MA, Zevallos JP & Nichols HB. Birth rates after radioactive iodine treatment for differentiated thyroid cancer. *International Journal of Cancer* 2017 **141** 2291–2295. (https://doi.org/10.1002/ijc.30917)

5 Sawka AM, Lakra DC, Lea J, Alshehri B, Tsang RW, Brierley JD, Straus S, Thabane L, Gafni A, Ezzat S, *et al.* A systematic review examining the effects of therapeutic radioactive iodine on ovarian function and future pregnancy in female thyroid cancer survivors. *Clinical Endocrinology* 2008 **69** 479–490. (https://doi.org/10.1111/j.1365-2265.2008.03222.x)

6 Vini L, Hyer S, Al-Saadi A, Pratt B & Harmer C. Prognosis for fertility and ovarian function after treatment with radioiodine for thyroid cancer. *Postgraduate Medical Journal* 2002 **78** 92–93. (https://doi.org/10.1136/pmj.78.916.92)

7 Albano D, Bertagna F, Panarotto MB & Giubbini R. Early and late adverse effects of radioiodine for pediatric differentiated thyroid cancer. *Pediatric Blood and Cancer* 2017 **64**. (https://doi.org/10.1002/pbc.26595)

8 Sarkar SD, Beierwaltes WH, Gill SP & Cowley BJ. Subsequent fertility and birth histories of children and adolescents treated with 131I for thyroid cancer. *Journal of Nuclear Medicine* 1976 **17** 460–464.

9 Dottorini ME, Vignati A, Mazzucchelli L, Lomuscio G & Colombo L. Differentiated thyroid carcinoma in children and adolescents: a 37-year experience in 85 patients. *Journal of Nuclear Medicine* 1997 **38** 669–675.

10 Nies M, Cantineau AEP, Arts EGJM, van den Berg MH, van Leeuwen FE, Muller Kobold AC, Klein Hesselink MS, Burgerhof JGM, Brouwers AH, van Dam EWCM, *et al.* Long-term effects of

Downloaded from Bioscientifica.com at 02/08/2025 12:32:54PM
via Open Access. This work is licensed under a Creative Commons
Attribution-NonCommercial-NoDerivatives 4.0 International License.
https://creativecommons.org/licenses/by-nc-nd/4.0/

radioiodine treatment on female fertility in survivors of childhood differentiated thyroid carcinoma. *Thyroid* 2020 **30** 1169–1176. (https://doi.org/10.1089/thy.2019.0560)

11 Metallo M, Groza L, Brunaud L, Klein M, Weryha G & Feigerlova E. Long-term quality of life and pregnancy outcomes of differentiated thyroid cancer survivors treated by total thyroidectomy and I(131) during adolescence and young adulthood. *International Journal of Endocrinology* 2016 **2016** 7586482. (https://doi.org/10.1155/2016/7586482)

12 Faddy MJ. Follicle dynamics during ovarian ageing. *Molecular and Cellular Endocrinology* 2000 **163** 43–48. (https://doi.org/10.1016/s0303-7207(99)00238-5)

13 Moolhuijsen LME & Visser JA. Anti-Müllerian hormone and ovarian reserve: update on assessing ovarian function. *Journal of Clinical Endocrinology and Metabolism* 2020 **105** 3361–3373. (https://doi.org/10.1210/clinem/dgaa513)

14 Hagen CP, Aksglaede L, Sørensen K, Main KM, Boas M, Cleemann L, Holm K, Gravholt CH, Andersson AM, Pedersen AT, *et al.* Serum levels of anti-Müllerian hormone as a marker of ovarian function in 926 healthy females from birth to adulthood and in 172 Turner syndrome patients. *Journal of Clinical Endocrinology and Metabolism* 2010 **95** 5003–5010. (https://doi.org/10.1210/jc.2010-0930)

15 Dewailly D, Andersen CY, Balen A, Broekmans F, Dilaver N, Fanchin R, Griesinger G, Kelsey TW, La Marca A, Lambalk C, *et al.* The physiology and clinical utility of anti-Mullerian hormone in women. *Human Reproduction Update* 2014 **20** 370–385. (https://doi.org/10.1093/humupd/dmt062)

16 Yaish I, Azem F, Gutfeld O, Silman Z, Serebro M, Sharon O, Shefer G, Limor R, Stern N & Tordjman KM. A single radioactive iodine treatment has a deleterious effect on ovarian reserve in women with thyroid cancer: results of a prospective pilot study. *Thyroid* 2018 **28** 522–527. (https://doi.org/10.1089/thy.2017.0442)

17 Evranos B, Faki S, Polat SB, Bestepe N, Ersoy R & Cakir B. Effects of radioactive iodine therapy on ovarian reserve: a prospective pilot study. *Thyroid* 2018 **28** 1702–1707. (https://doi.org/10.1089/thy.2018.0129)

18 WHO Adolescent health [Internet]. Available at: https://www.who.int/southeastasia/health-topics/adolescent-health (Accessed on January 28 2023).

19 Francis GL, Waguespack SG, Bauer AJ, Angelos P, Benvenga S, Cerutti JM, Dinauer CA, Hamilton J, Hay ID, Luster M, *et al.* Management guidelines for children with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2015 **25** 716–759. (https://doi.org/10.1089/thy.2014.0460)

20 WHO Scientific Group on Research on the Menopause in the 1990s. *Geneva S, Organization WH. Research on the Menopause in the 1990s: Report of a WHO Scientific Group* [Internet]. World Health Organization, p. 1996 1994. Available at: https://apps.who.int/iris/handle/10665/41841

21 Jopling H, Yates A, Burgoyne N, Hayden K, Chaloner C & Tetlow L. Paediatric anti-Müllerian hormone measurement: male and female reference intervals established using the automated Beckman Coulter Access AMH assay. *Endocrinology, Diabetes and Metabolism* 2018 **1** e00021. (https://doi.org/10.1002/edm2.21)

22 van Velsen EFS, Visser WE, van den Berg SAA, Kam BLR, van Ginhoven TM, Massolt ET & Peeters RP. Longitudinal analysis of the effect of radioiodine therapy on ovarian reserve in females with differentiated thyroid cancer. *Thyroid* 2020 **30** 580–587. (https://doi.org/10.1089/thy.2019.0504)

23 Piek MW, Postma EL, van Leeuwaarde R, de Boer JP, Bos AME, Lok C, Stokkel M, Filipe MD & van der Ploeg IMC. The effect of radioactive iodine therapy on ovarian function and fertility in female thyroid cancer patients: a systematic review and meta-analysis. *Thyroid* 2021 **31** 658–668. (https://doi.org/10.1089/thy.2020.0356)

24 Khvostunov IK, Nasonova E, Krylov V, Rodichev A, Kochetova T, Shepel N, Korovchuk O, Kutsalo P, Shegai P & Kaprin A. Cytogenetic damage induced by radioiodine therapy: a follow-up case study. *International Journal of Molecular Sciences* 2023 **24** 5128. (https://doi.org/10.3390/ijms24065128)

25 Mittica M, Dotto A, Comina M, Teliti M, Monti E & Giusti M. Cross-sectional and prospective study on anti-Müllerian hormone changes in a cohort of pre-menopausal women with a history of differentiated thyroid cancer. *Thyroid Research* 2020 **13** 1. (https://doi.org/10.1186/s13044-020-0075-z)

26 Scheffer JAB, Scheffer B, Scheffer R, Florencio F, Grynberg M & Lozano DM. Are age and anti-Müllerian hormone good predictors of ovarian reserve and response in women undergoing IVF? *JBRA Assisted Reproduction* 2018 **22** 215–220. (https://doi.org/10.5935/1518-0557.20180043)

Downloaded from Bioscientifica.com at 02/08/2025 12:32:54PM
via Open Access. This work is licensed under a Creative Commons
Attribution-NonCommercial-NoDerivatives 4.0 International License.
https://creativecommons.org/licenses/by-nc-nd/4.0/