Menopausal Age of Differentiated Thyroid Carcinoma Patients after Single Dose of Radioiodine Therapy –Single Institute based Experience

[1]Samira Sharmin, [2]Syed Muhammad Baqui Billah, [1]Hosne Ara Rahman, [1]Afroza Naznin, [1]Farida Yasmin, [2]Md. Monir Uddin

[1] Institute of Nuclear Medicine and Allied Sciences, SSMCH, Mitford, Dhaka.
[2] Sher-e-Bangla Medical College, Barishal
[3] District Sadar Hospital, Narsingdi

Correspondence Address : Dr. Samira Sharmin, PMO, INAMS, Mitford, Dhaka. Email:Samira958@gmail.com

ABSTRACT

Background: Menopause is a natural and unavoidable circumstance in all women's lives. Radioiodine therapy is the most popular method of treatment for differentiated thyroid carcinoma (DTC) worldwide. Considering these two, this study was designed to evaluate the menopausal age of DTC patients after a single dose of radioiodine therapy.

Patients and Methods: This is a retrospective study analyzed in INMAS, Mitford, Dhaka, from January 2018 to December 2019 among 225 female patients with DTC who were referred for radioiodine therapy of different doses according to their clinical state (75 mci (2.7 GBq), 100 mci (3.7 GBq), and 150 mci (5.5 GBq).

Results: Among 225 patients, about 47 women (20.9%) experienced menopause after radioiodine therapy during this study period. The average age of menopause in Bangladeshi women is 46.7 years (95% CI). In this study, the mean menopausal age of the study subjects was 44.1±2.6 years. About 13 patients experienced menopause after 75 mci (2.7 GBq) radioiodine therapy with a mean age of 45.6±2.2; 28 patients had menopause after receiving 100 mci (3.7 GBq) with a mean age of 44.4±2.7; and 6 patients had menopause after receiving 150 mci (5.5 GBq) of I-131 with a mean age of 44.1±2.0. The result was significant ($P<0.05$).

Conclusion: This study reveals that the mean menopausal age of the patients after radioiodine therapy is lower than the mean menopausal age of normal Bangladeshi women.

Keywords: Menopause, Radioiodine therapy, Differentiated Thyroid Carcinoma

Bangladesh J. Nucl. Med. Vol. 26 No. 2 July 2023
DOI: https://doi.org/10.3329/bjnm.v26i2.71474

INTRODUCTION

Thyroid carcinoma is a common malignancy all over the world. Treatment of thyroid carcinoma has multiple stages, and radioiodine therapy is one of the most efficient methods of treatment for thyroid carcinoma (1, 2). The incidence of thyroid carcinoma is increasing with time, and the use of radioiodine for the ablation of residual thyroid tissue and distant metastases has increased day by day (2). Thyroid carcinoma mostly observed among the younger female patients who has reproductive issue and go through a long menstrual life (3). At the time of radioiodine therapy all the human cell goes through radiation effect especially on the gonadal cells and has drawn special attention as gonads are affected over time which plays important impact residual life of patient (1,3,4). Menopause is a normal physiological phenomenon in every woman's life. Radioiodine therapy has an effect on menstrual status (3, 4). This study was designed to evaluate the menopausal status of women after being treated with a single dose of radioiodine therapy.

PATIENTS AND METHODS

A retrospective study was conducted among the women who were diagnosed with thyroid carcinoma and had a total thyroidectomy. About 225 patients were enrolled in this study who had received a single dose of radioiodine therapy after TSH stimulation and had taken regular follow-up with thyroid stimulating hormone (TSH), thyroglobulin (Tg), anti-Tg antibodies, and whole-body iodine scans (WBS). The study subjects didn't suffer from any distant metastases, and they had an almost regular menstrual cycle. The menopausal study subjects enrolled in this study had not had a menstrual cycle for at least twelve consecutive months and had different symptoms of menopause, such as hot flashes

and sleeping disturbances (5). The data were compiled and analyzed by SPSS version 22.

RESULT

A total of 47 women (20.9%) experienced menopause after radioiodine therapy during this study period. The average age of menopause in Bangladesh is 46.7 years (95% CI) (6). At the beginning of the study, the mean age of all the study subjects was 31.2±6.1 years, with range of 17~52 years. The mean age of the menopausal age group was 37.8±5.1 years, and menstruating women's mean age was 25.1±4.1 years. At the end of the study, the mean menopausal age and menstruating age of the study subjects were respectively 44.1±2.6 years and 32.4±5.2 years.

Table 1: Characteristics of the study subjects

Status	Menopause	No menopause/cycling/menstruating
Study Subjects	47(20.9%)	178 (79.1%)
Mean Age	During the beginning of the study	
	37.8±5.1 years	25.1±4.1 years
	During end of the study	
	44.1±2.6 years	34.2±5.2 years
Type of carcinoma	Papillary (46) & Follicular (1)	Papillary (178)
TSH	0.01± 0.01 mlU/L	0.01±0.01 mlU/L
Thyroglobulin	1.26±0.2 ng/ml	1.07±0.5 ng/ml
AntiTg antibody	1.25±1.3IU/mL	1.09±1.1IU/mL
Whole body scan	Negative	Negative

After radioiodine therapy, patients experienced menopause within 250 months. And most of the patients became menopausal after 100 months of radioiodine therapy.

This study also revealed that during this study period, about 37 patients got 75 mci (2.7 GBq) of radioiodine, and among them, about 13 patients experienced menopause with a mean age of 45.6±2.2. 150 patients received 100

Table 2: Number of patients according to the dose of radioiodine therapy.

Dose (mci)	Frequency	Percent (%)
75 mci(2.7GBq)	37	16.4%
100 mci(3.7GBq)	150	66.7%
150 mci(5.5GBq).	38	16.9%
Total	225	

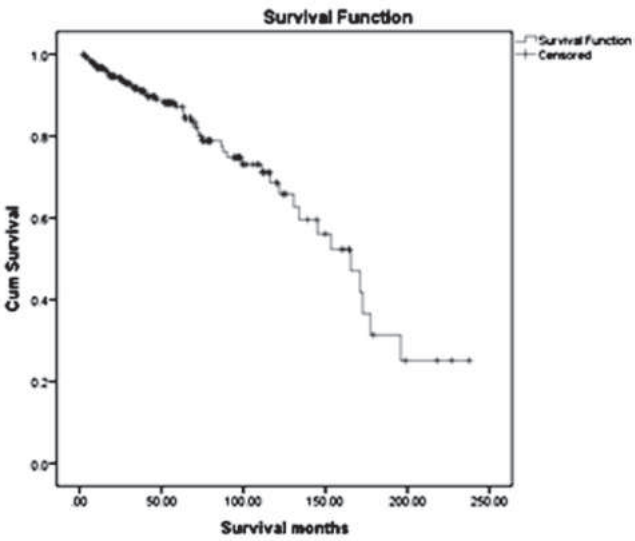

Fig 1: Kaplan Meier survival curve shows menopausal events after Radioiodine therapy among cycling women.

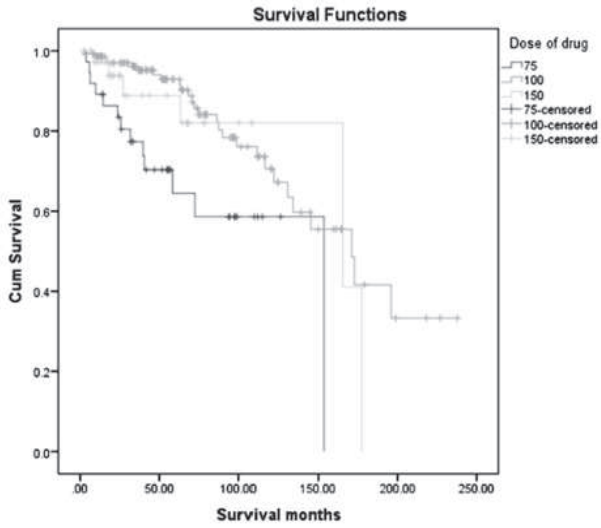

Fig 2: Kaplan Meier survival curve shows menopausal events after Radioiodine therapy among cycling women according to the dose.

mci (3.7 GBq) radioiodine therapy; among them, 28 patients had menopause with a mean age of 44.4±2.7; and 38 patients received 150 mci (5.5 GBq) radioiodine therapy; among them, 6 patients had menopause with a mean age of 44.1±2.0. The result was significant (P<0.05).

DISCUSSION

Thyroid carcinoma patients can lead a normal life and an almost disease-free survival state with the treatment of radioiodine therapy. It is a very popular method of treatment for this reason (1). Menopause is part and parcel of a woman's life. Radioiodine has side effects on the female reproductive system, such as disturbance of the menstrual cycle and menopause (2-4, 6, 7).

In this study, the mean age of all the study subjects was 31.2±6.1 years with range of 17~52 years, and the mean age of the menopausal age group was 37.8±5.1 years. Menstruating women's mean age was 25.1±4.1 years at the beginning of the study. At the end of the study, the mean menopausal age of the study subjects was 44.1±2.6 years, and that of menstruating women was 34.2±5.2 years. Similar findings were observed in a study conducted by Ceccarelli et al. (2001) (3), which found the mean age of the study subjects at the beginning was 39.2±4.9 years and at the end of the study was 52.9±5.1 years. Another study conducted by Martins et al. (2011) also showed the mean menopausal age of the study subjects was 49.3±3.8 years, which was consistent with the present study (4). Another study conducted by Rosario (2012) found that the mean age of the study subjects was 44.4 years, which was similar to the present study (7).

The menopausal age found in this study was slightly lower than the average menopausal age of Bangladeshi women. A study conducted by Sibli et al. (2022) showed that the average age of the menopausal age of Bangladeshi women was 46.7 years (95% CI) (6), whereas this study showed that the mean age of the study subjects was 44.1±2.6 years.

This study also revealed that during this study period, about 37 patients got 75 mci (2.7 GBq) of radioiodine, and among them, about 13 patients experienced menopause with a mean age of 45.6±2.2. 150 patients received 100 mci (3.7 GBq) radioiodine therapy; among them, 28 patients experienced menopause with a mean age of 44.4±2.7; and 38 patients received 150 mci (5.5 GBq) radioiodine therapy; among them, 6 patients had menopause with a mean age of 44.1±2.0 years. The result was statistically significant (P value <0.05, T-test).

Similar findings were also noticed in a study conducted by Sawka et al. (2008) that earlier onset of menopause was noticed in women with treated I-131 for thyroid carcinoma than in women not treated with radiation (8). It was found in a study that I-131 therapy might contribute to follicular atresia and induce an earlier onset of menopause (3).

Moreover, it had been suggested in a study that the 3.7 GBq dose might be the cause of the earlier onset of menopause, and more than 3.7 GBq increased the risk (9).

Radiation had an effect on the gonads of the human being, especially the ovaries, which were a substantial risk for exposure. The oocyte is very radiosensitive, with an estimated LD50 of <2 Gy, and the individual oocyte is highly radiosensitive, with a value of 0.12 Gy (10). Radioiodine might affect the ovaries because radioiodine circulates within the blood, bowel, and bladder before sequestration from the body (8, 9, 11). This study showed that all the women reached menopause within 250 months after radioiodine therapy. Sioka& Fotopoulos also found similar findings in their study and showed that those who received radiation doses experienced earlier menopause than those who had not received radioiodine treatment during their menstruating age (11). Few studies also showed that menstrual irregularities also increased with the increasing age of the patients who received radioiodine therapy (12, 13).

A few studies suggest that emotional and physical stress alter endocrine function, which changes the hypothalamic and pituitary axes, which can lead to menstrual cycle changes as well as an earlier onset of menopause (14). A study conducted by Rosario found that stress had an effect on hypothalamic dysfunction and played a role in menstrual abnormalities (7).

CONCLUSION

Radioiodine therapy reduces the mortality and morbidity of carcinoma and thyroid patients.However, this study revealed that it causes an earlier onset of menopause in cycling women who received radioiodine therapy for thyroid carcinoma.

LIMITATIONS

Here, all the patients were in a menopausal state and had amenorrhea for at least 12 consecutive months (5) with clinical symptoms (hot flash, mood change, sleep disturbance, etc.); moreover, no hormonal correlation was found during the study period (FSH, LH).

REFERENCES

1. Zhai M, Zhang D, Long J, Gong Y, Ye F, Liu S, Li Y. The global burden of thyroid cancer and its attributable risk factor in 195 countries and territories: A systematic analysis for the Global Burden of Disease Study. Cancer medicine. 2021 Jul;10(13):4542-54.
2. Nguyen QT, Lee EJ, Huang MG, Park YI, Khullar A, Plodkowski RA. Diagnosis and treatment of patients with thyroid cancer. American health & drug benefits. 2015 Feb;8(1):30.
3. Ceccarelli C, Bencivelli W, Morciano D, Pinchera A, Pacini F. 131I therapy for differentiated thyroid cancer leads to an earlier onset of menopause: results of a retrospective study. The Journal of Clinical Endocrinology & Metabolism. 2001 Aug 1;86(8):3512-5.
4. Martins T, Azevedo T, Martinho M, Oliveira S, Neto J, Rodrigues F. Radiodine therapy and age at menopause in women with differentiated thyroid cancer. InEndocrine Abstracts 2011 Apr 1 (Vol. 26). Bioscientifica.
5. Utian WH. Menopause-related definitions. International Congress Series 2004 Apr 1 (Vol. 1266, pp. 133-138). Elsevier.
6. Sibli MS, Islam S, Uddin MJ, Ali MY, Biswas R, Akter S, Islam MS. Analysis of the average menopause age of Bangladeshi women: A public health perspective. World Journal of Advanced Research and Reviews. 2022;16(3):231-5.
7. Rosario MD, Jasul Jr GV. Changes in Ovarian Function after Radioactive Iodine among Patients with Differentiated Thyroid Carcinoma at St. Luke's Medical Center, Philippines. Journal of the ASEAN Federation of Endocrine Societies. 2012;27(1):63.
8. Sawka AM, Lakra DC, Lea J, Alshehri B, Tsang RW, Brierley JD, Straus S, Thabane L, Gafni A, Ezzat S, George SR. A systematic review examining the effects of therapeutic radioactive iodine on ovarian function and future pregnancy in female thyroid cancer survivors. Clinical endocrinology. 2008 Sep;69(3):479-90.
9. Rosário PW, Fagundes TA, Fagundes AV, Barroso ÁL, Rezende LL, Padrão EL, Guimarães VC, Purisch S. Radioiodine therapy and age at menopause in patients with thyroid cancer. Clinical endocrinology. 2006 Feb;64(2):225-6.
10. Duncan FE, Kimler BF, Briley SM. Combating radiation therapy-induced damage to the ovarian environment. Future Oncology. 2016 Jul;12(14):1687-90.
11. Sioka C, Fotopoulos A. Effects of I-131 therapy on gonads and pregnancy outcome in patients with thyroid cancer. Fertility and sterility. 2011 Apr 1;95(5):1552-9.
12. Rosário PS, Fagundes TA, Fagundes AV, Barroso ÁL, Rezende LL, Padrão EL, Guimaraes VC, Horta AC, Franco M, Purisch S. Ovarian function after radioiodine therapy in patients with thyroid cancer. Experimental and clinical endocrinology & diabetes. 2005 Jun;113(06):331-3.
13. 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 Feb;78(916):92-3.
14. Kronenberg HM. Williams Textbook of Endocrinology E-Book. Elsevier Health Sciences; 2007 Nov 30