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Original Article

Incidence of Radiation-Induced Hypothyroidism among Head and Neck Cancer Patients

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ABSTRACT

Background: Inadvertent radiation exposure to the thyroid gland during radiotherapy may lead to primary hypothyroidism, adding to the morbidity and mortality in cancer patients. The present study was carried out to analyze the incidence of hypothyroidism after radiotherapy at a tertiary care center.

Methods: A retrospective study was carried out among 60 patients undergoing radiotherapy for head and neck cancers in from Jan 2024 to Dec 2024. Thyroid levels were evaluated pre-radiotherapy and were followed up till 12 months post-radiotherapy. Data was coded and entered to Microsoft Excel. Data was analysed using SPSS 22.0 software.

Results: Of the 60 patients, the mean age was 44.1 ± 15.6 years, 47 were males (78.3%) and 13 females (21.7%). All patients were euthyroid prior to initiation of radiotherapy. No cases of hypothyroidism were detected at 1 month or 3 months following completion of radiotherapy. At 6 months, 12 patients (20.0%) developed hypothyroidism. At 12 months, the incidence increased to 19 patients (31.7%). Female patients demonstrated a higher incidence of hypothyroidism compared to male patients at both 6- and 12-months post-radiotherapy. The mean age of patients who developed hypothyroidism was 36.8 ± 14.2 years, with female patients developing hypothyroidism at a younger mean age compared to male patients.

Conclusion: The incidence of radiation therapy-induced hypothyroidism is found to be 31.67%. It is imperative that thyroid function monitoring should be taken as a routine procedure following radiation therapy to pick up subclinical/clinical hypothyroidism early, start appropriate treatment and avoid complications.

Keywords: *radiation therapy, hypothyroidism, head and neck cancer, radiation injury, risk factors.*

INTRODUCTION

Head and neck cancer is the sixth leading cancer globally according to its incidence.[1] The different treatment modalities available for cancer are: surgery, radiotherapy, chemotherapy or multimodality methods.[2] While early-staged cancers (T1 or T2) are treated with a single modality— such as radiation therapy or surgery, in locally advanced head and neck cancer radiotherapy with or without chemotherapy is the major treatment modality.[3,4] As is the case with head and neck cancer, most tumors are locoregionally advanced at the time of diagnosis.[5] Thus, radiotherapy includes the primary site of the tumor and often the entire neck, including the thyroid gland falling within the radiation field.[6] Inadvertent radiation exposure to the thyroid gland during radiotherapy may lead to primary hypothyroidism—a common late endocrine complication.[7] Literature reports that around 10%–50% of patients develop hypothyroidism after radiation to the head and neck using fields that include all or part of the thyroid gland.[8] Younger age females and addition of chemotherapy or neck surgery are the possible risks factors for the development of hypothyroidism. Additionally, it has been reported that risk of hypothyroidism increases with higher radiation volume or in cases of bilateral neck irradiation.

Though the approximate time after radiotherapy for the development of hypothyroidism is not yet defined, it has been observed that most cases occur within first three years of radiotherapy. Among adults exposed to radiation in the thyroid region, it is estimated that only 5% develop symptomatic clinical hypothyroidism. The underlying pathology related to radiation-induced hypothyroidism are theorized to be: vessel damage, fibrosis of capsule of the gland or autoimmune reaction.[9,10] Such a complication can result in impaired quality of life in cancer patients; altered metabolism, fatigue, decreased overall health perception, cognitive impairment, worse emotional well-being, and sexual dysfunction are few impairments among others.[11,12] Hypothyroidism also increases the overall risk of mortality.[13] Thus, it becomes important to estimate the incidence, identify the risk factors, explore the different treatment modalities of radiation-induced hypothyroidism among cancer patients to improve their health outcomes and overall quality of life. Hence, the present study was carried out to analyze the incidence of hypothyroidism after radiotherapy at a tertiary care center in Kulasekaram in Kanyakumari District

METHODS

Study design: Retrospective observational study

Study population: Head and neck cancer patients receiving radiotherapy at a tertiary care centre Sree Mookambika Institute of Medical Sciences.

Study period: Jan 2024-dec 2024

Inclusion Criteria: Adult patients ≥18 years, histologically confirmed head and neck cancer, receiving radical radiotherapy.

Exclusion Criteria: Pre-existing thyroid disease, prior thyroid surgery, incomplete follow-up.

Data Collection Procedure

After obtaining written informed consent, patients included in the study were evaluated for thyroid function tests including TSH, free T3 and free T4 before the start of radiation therapy, and followed up at 1 month, 3 months, 6 months, and 12 months after radiotherapy. The patients detected with altered thyroid function were referred and further managed by the medicine department. The cases underwent IMRT with radiotherapy. Post operative patients received 6000cGy and patients who underwent radical treatment without surgery will receive 6600cGy. Informed consent was obtained from each participant before data collection.

Statistical Analysis

Data was coded and entered to Microsoft Excel. Data was analysed using SPSS 22.0 software. Categorical variables were presented in frequencies and percentages and quantitative variables were expressed as mean and standard deviation. Association between thyroid dysfunction and radiotherapy were tested using Chi-square. Significance level was fixed at a p value of <0.05.

RESULTS

Out of 65 patients screened, 5 were excluded (2 with pre-existing hypothyroidism and 3 due to irregular follow-up). A total of 60 patients were included for final analysis. The mean age was 44.1 ± 15.6 years (range: 18–78 years). There were 47 males (78.3%) and 13 females (21.7%). Eighteen patients (30%) received 6000 cGy, while forty-two patients (70%) received 6600 cGy. Thyroid gland doses ranged from 4100 to 6400 cGy (Table 1). All patients were euthyroid prior to initiation of radiotherapy. No cases of hypothyroidism were detected at 1 month or 3 months following completion of radiotherapy. At 6 months, 12 patients (20.0%) developed hypothyroidism. At 12 months, the incidence increased to 19 patients (31.7%) (Table 2). Female patients demonstrated a higher incidence of hypothyroidism compared to male patients at both 6- and 12-months post-radiotherapy. The time interval was calculated from the date of completion of radiotherapy. The age-wise distribution of hypothyroidism at 12 months post-radiotherapy is shown in Table 3. Higher incidence was observed among patients aged 18–20 years and 61–80 years. The mean age of patients who developed hypothyroidism was 36.8 ± 14.2 years, with female patients developing hypothyroidism at a younger mean age compared to male patients.

Table 1. Characteristics of study participants (n = 60)

Variable	Frequency	Percentage
Gender		
Male	**47**	**78.3**
Female	**13**	**21.7**
Primary tumor site		
Oral cavity	19	**31.67**
Oropharynx	10	16.67
Hypopharynx	8	13.33

Larynx	10	16.67
Nasopharynx	6	10
MUO Neck	2	3.33
Others (salivary gland, sinonasal, etc.)	5	8.33
Dose of radiation received		
6000 cGY	18	30
6600 cGY	42	70

Table 2. Incidence of hypothyroidism following head and neck radiotherapy

Post-radiotherapy interval	Total cases (n=60)	Percentage (%)	Male (n=32)	Percentage (%)	Female (n=28)	Percentage (%)
1 month	0	0	0	0	0	0
3 months	0	0	0	0	0	0
6 months	12	20.0	5	15.6	7	25.0
12 months	19	31.7	8	25.0	11	39.3

Table 3. Age-wise distribution of hypothyroidism at 12 months post-radiotherapy

Age group (years)	Total patients	Hypothyroid patients	Percentage (%)
18–20	2	1	50.00
21–40	7	1	14.29
41–60	27	7	25.93
61–80	24	10	41.67
Total	**60**	**19**	**31.67**

DISCUSSION

The incidence of hypothyroidism following radiation exposure in head and neck cancer patients has been variously reported to be between 10-50%.[8,14] The present study reports an incidence of 31.67%, within the range reported in literature. The time of occurrence also differs widely—few studies reporting that radiation therapy induced hypothyroidism occurring relatively shortly after the therapy (within months), while others suggest that changes in function may occur for multiple years following treatment.[15,16] In the present study, no cases of hypothyroidism were detected at 1 month or 3 months following completion of radiotherapy. At 6 months, 12 patients (20.0%) developed hypothyroidism and at 12 months, there were 19 patients (31.7%) with hypothyroidism. Female patients demonstrated a higher incidence of hypothyroidism compared to male patients at both 6- and 12-months post-radiotherapy. The time interval was calculated from the date of completion of radiotherapy. This is in line with other studies that report younger age females as a possible risks factor for the development of hypothyroidism.[14,17,18] Again, opinion is divided on the association of age with development of hypothyroidism. Das et al. in their study reported a mean age of 52 years, and that there was no effect of age on hypothyroidism incidence.[19]

Muzumdar et al. reported that among the patients who developed hypothyroidism, nine of 14 were in the age group of 51 to 60 years ($P = 0.0522$), which was statistically significant.[20] In the present study higher incidence was observed among patients aged 41-60 years and 61–80 years. The present study has few limitations. Firstly, it was a single-center study which limits the generalizability of the results. Further studies with larger sample sizes and longer follow-up periods are warranted. Also, subclinical hypothyroidism was not studied; patients may develop subclinical hypothyroidism following radiotherapy, with elevated TSH levels with normal or low normal free T4 levels without any symptoms. The relationship between the dose/type of radiation therapy techniques and incidence of hypothyroidism was also not studied. Patients treated with 2-D technique are shown to have higher chances of developing hypothyroidism than those treated with 3-DCRT and IMRT techniques.[1] Currently, there are no consensus guidelines from leading radiotherapy groups regarding optimal screening and management practices for radiation therapy induced hypothyroidism.[14] Nevertheless, it is imperative that thyroid function monitoring should be taken as a routine procedure following radiation therapy to pick up subclinical/clinical hypothyroidism early, start appropriate treatment and avoid complications.

CONCLUSION

The incidence of radiation therapy-induced hypothyroidism is found to be 31.67%. No cases of hypothyroidism were detected at 1 month or 3 months following completion of radiotherapy. At 6 months, 12 patients (20.0%) developed hypothyroidism and at 12 months, there were 19 patients (31.7%) with hypothyroidism. Female patients demonstrated a higher incidence of hypothyroidism compared to male patients at both 6- and 12-months post-radiotherapy.

DECLARATIONS

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Conflict of Interest
The authors declare that they have no conflict of interest.

Ethics Approval
The study was approved by the Institutional Ethics Committee of Sree Mookambika Institute of Medical Sciences.

Consent to participate
As this was a retrospective record-based study using anonymized data, the requirement of informed consent was waived by the Institutional Ethics Committee

Consent to publish
Not applicable. The manuscript does not contain any individual person's data in any form

Author Contributions
K.L. Jayakumar: Conceptualization, Methodology, Supervision, Validation, Critical revision of manuscript. K. Kanmani: Data curation, Formal analysis, Investigation, Writing – original draft preparation, Writing – review & editing. All authors read and approved the final manuscript

Availability of Data and Materials
The datasets generated and/or analysed during the current study are not publicly available due to institutional data protection policies but are available from the corresponding author on reasonable request, subject to approval by the Institutional Ethics Committee.

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