RESEARCH ARTICLE

Editorial Process: Submission:05/17/2025 Acceptance:10/04/2025 Published:10/17/2025

Thyroid Dysfunction Following Exposure to Therapeutic Doses of External Beam Radiotherapy in Head and Neck Cancer

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Abstract

Background: Head and neck cancers are among the most common cancers worldwide and particularly prevalent in India. These malignancies often necessitate a multimodal treatment approach, with radiotherapy being a cornerstone of management. This study aims to investigate the incidence and nature of thyroid dysfunction in patients undergoing external beam radiotherapy (EBRT) for head and neck cancer, highlighting the critical need for routine thyroid function assessments in this population. **Methods:** A prospective observational study was conducted over two years, from April 2022 to April 2024, at the Department of Radiation Oncology, Government Medical College, Srinagar. The study enrolled 63 newly diagnosed head and neck cancer patients who met specific inclusion criteria. Comprehensive pre-treatment evaluations, including thyroid function tests (TFTs), were performed prior to initiating treatment. Patients received conformal radiotherapy, with careful planning to minimize thyroid exposure, and TFTs were monitored immediately post-treatment and at three-month intervals for six months. **Results:** The cohort comprised predominantly male patients (79.4%) with a median age of 60 years. The most common histological type was squamous cell carcinoma (87.3%), and advanced stages (III and IV) were prevalent at diagnosis, accounting for 63.5% of cases. A total of 29 patients (46%) developed hypothyroidism during follow-up, with 22 patients (75.9%) diagnosed with subclinical hypothyroidism and 7 patients (24.1%) with overt hypothyroidism. At three months post-radiation, 9 patients exhibited subclinical hypothyroidism, while no cases of overt hypothyroidism were observed. By six months, the numbers increased to 11 for subclinical and 5 for overt hypothyroidism, and by nine months, an additional 2 patients developed both forms. Analysis showed a significant increase in TSH levels over time ($p < 0.05$), indicating thyroid dysfunction. Although the mean free T4 levels exhibited a non-significant decrease, a notable trend was observed regarding thyroid volume and radiation dose. Patients who developed hypothyroidism had a lower mean thyroid volume (11.83 cm^3) compared to the euthyroid group (13.80 cm^3). Furthermore, while the mean radiation dose to the thyroid gland was higher in the hypothyroid group (48.40 Gy vs. 45.30 Gy), this difference did not reach statistical significance. However, a higher radiation dose (>60 Gy) correlated with an increased incidence of hypothyroidism, suggesting a potential dose-response relationship. **Conclusion:** This study highlights a significant incidence of hypothyroidism (46%) in patients treated for head and neck cancer with radiotherapy. The findings suggest that radiotherapy can impair thyroid function through direct tissue damage and vascular injury, necessitating regular thyroid function monitoring in affected patients. Future research should focus on larger, multi-institutional studies with extended follow-up to better understand the long-term impacts of radiotherapy on thyroid health and to develop comprehensive management strategies for this treatment-related side effect.

Keywords: Head and Neck cancer- Radiotherapy- Thyroid Dysfunction- EBRT- IMRT- VMAT.

Asian Pac J Cancer Prev, **26 (10)**, 3841-3848

Introduction

The term “head and neck cancer” (HNC) encompasses cancers affecting the upper aerodigestive tract, including the lips, oral cavity, oropharynx, sinonasal cavities, larynx, hypopharynx, and salivary glands, collectively representing 6% of all cancers [1]. Head and neck cancer is predominantly a loco-regional disease with less than 5% of patients having distant metastases at diagnosis. Around 60% of patients have locally advanced disease (i.e. stage III and VI) at diagnosis [2]. The main treatment options are surgery and radiotherapy (RT), either alone or in combination, and in recent years with addition of chemotherapy, RT is the primary treatment for head and neck cancers [3], thus 70% of patients receive primary RT and 30% receive surgery with or without post-operative RT [4]. For the majority of patients with early stage HNSCC, single modality treatment may be sufficient for cure.

Over the past three decades there has been a significant technological development in the delivery of radiation,

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from two-dimensional (2D)-RT based on X-ray images to CT-based three-dimensional conformal treatment (3D-CRT). 3D-CRT uses multiple treatment fields to deliver a homogeneous dose to the target area, and subsequent implementation of multi-leaf collimators and more advanced computer algorithms, has enabled intensity modulated RT (IMRT) and later volumetric modulated arc therapy (VMAT). With these novel treatment techniques there is potential for sparing the normal tissues while increasing radiation dose to the tumor and other target areas [5-7].

Patients who receive radiotherapy to the neck are at increased risk of developing thyroid dysfunction, which is usually seen in the form of biochemical hypothyroidism but may also present as overt hypothyroidism. These patients are also more likely to develop both benign and malignant nodules of the thyroid gland [8]. Thyroid dysfunction after radiation is most often manifested by elevated serum concentration of Thyroid stimulating hormone (TSH). Damage to the thyroid gland by ionizing radiation is due to a variety of pathological mechanisms. These include vascular effects in the epithelium of small vessels and the development of fibrosis of capsular structures, while the damage to the follicular epithelial cells is considered less important [9, 10]. The mechanisms for radiation-induced hypothyroidism are largely unknown but are assumed to be related to vascular damage [10].

Aims and Objectives

The primary objective of this study was to estimate the incidence of thyroid dysfunctions in head and neck cancer patients receiving radiation therapy. Secondary objectives included exploring the association between radiation dose and thyroid dysfunction and emphasizing the necessity of including thyroid function tests (TFTs) in early follow-up for patients undergoing external beam radiation therapy (EBRT).

Materials and Methods

This prospective observational study was conducted over two years (April 2022–April 2024) in the Department of Radiation Oncology at Government Medical College, Srinagar. The study included newly diagnosed head and neck cancer patients with normal thyroid function and intact thyroid glands. Patients with a history of thyroid surgery, pre-existing thyroid disorders, previous head and neck radiotherapy, or recurrent cancers were excluded.

Patients underwent detailed ENT examinations, histopathological confirmation, imaging (CEMRI, CECT, or PET-CT), and baseline assessments, including TFTs, thyroid ultrasound, and other preparatory tests. EBRT was delivered using VMAT/IMRT with a dose constraint of <45 Gy to the thyroid gland which had less priority over PTV. Thyroid function was monitored immediately post-treatment and at three-month intervals for minimum of six months.

Results

The study analyzed 63 patients with head and neck cancer treated using definitive conformal radiotherapy. The median age was 60 years, ranging from 26 to 80 years, with most patients falling into the 61–70 age group (33.3%), followed by the 51–60 age group (25.4%), collectively accounting for 58.7% of the population. Male patients formed the majority (79.4%), and 73% were smokers. The most common diagnosis was carcinoma glottis (49.2%), followed by oral cavity malignancies (19.1%). The predominant histology was squamous cell carcinoma (87.3%), with a smaller proportion of mucoepidermoid and adenoid cystic carcinoma cases (6.3% each). Most patients presented with advanced-stage disease, with 33.3% at Stage IV and 30.2% at Stage III. The mean thyroid volume was 12.19 cm^3, ranging from 5.5 to 18.2 cm^3.

All patients received radiotherapy to the head and neck, with 41.3% undergoing exclusive radiotherapy and 58.7% receiving concurrent chemoradiotherapy (CCRT). Cisplatin was the most commonly used concurrent chemotherapy (97.3%), with carboplatin administered in patients with reduced creatinine clearance (2.7%). Radiation was delivered using VMAT in 92.1% of patients and IMRT in 7.9%, with a mean dose of 66.46 Gy delivered over 30–35 fractions. The radiation dose to the thyroid gland ranged from 0.24 Gy to 68.94 Gy, with a mean dose of 46.72 Gy.

The median follow-up period was nine months, with 58.7% completing nine months and 28.6% completing 12 months of follow-up. Eight patients (12.7%) expired after six months of follow-up. Radiation-induced hypothyroidism (either subclinical or overt) was observed in 46% of patients, with 29 developing hypothyroidism and 34 remaining euthyroid. Among hypothyroid patients, 22 (75.9%) had subclinical hypothyroidism, and 7 (24.1%) developed overt hypothyroidism. At three months post-radiation, nine patients had subclinical hypothyroidism, with no cases of overt hypothyroidism. By six months,

Table 1. Patient Profile and Disease Characteristics

Patient Profile (n= 63)				
Age	Median age= 60 years		Range= 26-80	
Gender	Male= 50 (79.4%)		Female = 13 (20.6 %)	
Diagnosis	Glottis = 31 (49.2 %)		Oral Cavity = 12 (19.1 %)	
	Salivary Gland=8 (12.7 %)		Supra Glottis= 6 (9.5%)	
	Hypopharynx= 4 (6.3%)		Nasopharynx=2 (3.2 %)	
Stage	I= 19%	II= 17.5%	III= 30.2%	IV= 33.3%
Thyroid volume (cm^3)	Mean= 12.19		Range= 5.5 – 18.2	

Table 2. Treatment Details of Patients and Follow-up. RT- Radiation, CCRT- Concurrent chemoradiotherapy, IMRT- intensity modulated radiotherapy, VMAT- volumetric modulated arc therapy.

Treatment Details (n=63)			
Treatment Modality	CCRT=37 (58.7%)		RT- Alone= 26 (41.3%)
Radiation Technique	VMAT=58 (92.1%)		IMRT= 5 (7.9%)
Radiation Dose to Neck	Mean=66.46 Gy		Range = 60-70 Gy
Concurrent Chemotherapy	Cisplatin=36 (97.3%)		Carboplatin=1 (2.7%)
Radiation Dose to Thyroid Gland	Mean=46.72 Gy		Range=0.24 – 68.9 Gy
Median Follow-up	6 months= 100%	9 months= 58.7%	12 months= 28.6%

11 patients developed subclinical hypothyroidism, and 5 developed overt hypothyroidism. At nine months, 2 patients were newly diagnosed with subclinical and 2 with overt hypothyroidism.

TSH levels showed a statistically significant increase at three, six, and nine months ($p < 0.05$), while free T4 levels exhibited no significant decline ($p > 0.05$). There was no significant correlation between hypothyroidism and patient age, sex, smoking history, cancer stage, histology, treatment modality, or radiation technique ($p > 0.05$). Hypothyroidism was slightly more prevalent among females (53.8%), patients receiving CCRT (51.3%), and

Table 3. Association with Hypothyroidism. (P<0.05 is statistically significant)

Association With Hypothyroidism With Patient, Disease And Treatment Profile								
Variables		No	Yes	Chi Test	P value	df	Table value	Result
Age	Up to 30 Years	2	0	3.214	0.667	5	11.07	Not Significant
	31-40 Years	3	3					
	41-50 Years	4	4					
	51-60 Years	8	8					
	61-70 Years	13	8					
	>70 Years	4	6					
Sex	Male	28	22	0.403	0.526	1	3.841	Not Significant
	Female	6	7					
Smoker	Yes	25	21	0.01	0.921	1	3.841	Not Significant
	No	9	8					
Disease(Diagnosis)	CA Glottis	16	15	4.535	0.716	7	14.067	Not Significant
	CA Hypopharynx	2	2					
	CA Oral Cavity	7	5					
	CA Salivary Gland	5	3					
	CA Supraglottis	4	2					
	CA Nasopharynx	1	1					
Disease (Hostology)	Adenoid Cystic Carcinoma	3	1	0.772	0.68	2	5.991	Not Significant
	Squamous Cell Carcinoma	29	26					
	Mucoepidermoid Carcinoma	2	2					
Stage	1	8	4	1.559	0.669	3	7.815	Not Significant
	2	5	6					
	3	11	8					
	4	10	11					
Treatment	CCRT	18	19	1.021	0.312	1	3.841	Not Significant
	RT ALONE	16	10					
Radiation (Technique)	IMRT	3	2	0.08	0.778	1	3.841	Not Significant
	VMAT	31	27					
Total Dose	60GY/30#	4	3	3.076	0.545	4	9.488	Not Significant
	66GY/33#	13	8					
	65.25GY/29#	2	2					
	70GY/35#	15	16					

RT, Radiation;CCRT, Concurrent chemoradiotherapy; IMRT, intensity modulated radiotherapy; VMAT, volumetric modulated arc therapy

Table 4. Association with Thyroid Volume (cm³). (P<0.05 is statistically significant)

Association of Hypothyroidism With Thyroid Volume (Cm³)									
Variables		Mean	SD	N	DF	T-test	P value	Result
Hypothyroidism	No	13.8	6	34	61	0.807	0.423	Not Significant
	Yes	11.83	7.15	29				

Table 5. Association with Mean Radiation Dose to Thyroid Gland. (P<0.05 is statistically significant)

Association Of Hypothyroidism With Radiation Dose To Thyroid (Mean)								
Variables		Mean	SD	N	DF	T-test	P Value	Result
Hypothyroidism	No	45.3	14.25	34	61	1.187	0.24	Not Significant
	Yes	48.4	16.27	29				

those treated with VMAT (46.6%). Patients receiving >60 Gy to the thyroid gland had a slightly higher incidence of hypothyroidism (46.42%) than those receiving ≤60 Gy (42.86%), though the difference was not statistically significant. The mean thyroid volume was higher in euthyroid patients (13.80 cm³ vs. 11.83 cm³), and the mean thyroid dose was slightly higher in the hypothyroid group (48.40 Gy vs. 45.30 Gy), but neither finding was statistically significant. Patients with thyroid dysfunction were managed under the care of an endocrinologist. No patients showed overt clinical symptoms of hypothyroidism, and all were monitored closely during follow-up.

Discussion

The thyroid gland was previously considered to be relatively radio resistant. However, it was seen that patients exposed to radiation such as those receiving radiation to the head and neck for treatment of cancers, those exposed to radiation as a result of nuclear accidents and the nuclear explosions in Hiroshima and Nagasaki, showed an increased incidence of thyroid dysfunction and thyroid cancers. The possible mechanism for thyroid dysfunction could be because of direct damage to parenchymal cells and indirectly through vascular injury [11]. Direct parenchymal injury becomes evident at around 12 months, however, vascular injury usually presents late. Radiation may inhibit specific functions of the follicular epithelium, reduce the number of functional follicles, alter vascular permeability and induce immunological damage. However, the exact mechanism is unknown [9].

The purpose of this study was to determine the incidence of thyroid dysfunctions in patients with head and neck cancer treated with conformal radiation and to explore the association of radiation dose to thyroid gland and thyroid dysfunction. The incidence of 46% at a median follow-up of 9 months clearly indicates that hypothyroidism is a significant effect after radiation to the neck. Radiation-induced hypothyroidism can either be primary hypothyroidism because of direct irradiation of the thyroid, and less often, central hypothyroidism because of irradiation of the hypothalamo-pituitary axis. The tolerance dose (TD) defined as TD 5/5 is the dose of radiation that could cause not more than 5% severe complication rates within 5 years after treatment. For the thyroid, it is considered 20 Gy when all or part of the gland is irradiated with conventional fractionation. Emami et al. [12] reported values of TD 8/5, TD 13/5, and TD 35/5 for whole thyroid irradiation as 45, 60, and 70 Gy, respectively, for the endpoint of clinical hypothyroidism. Kehwar [13] confirmed the calculated TD 5/5 for the thyroid as 45 Gy for clinical thyroiditis.

In our study, all patients had a minimum follow-up of 6 months. Follow-up ranged from 6 months to 12 months with a median follow-up of 9 months. Kim et al.

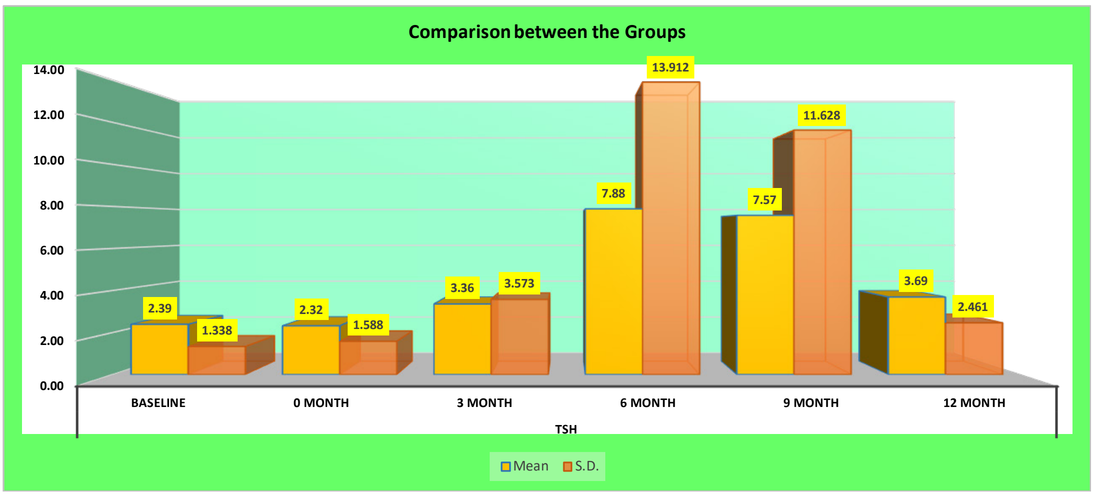

Figure 1. Mean TSH Levels during Follow-up

[14] had a median follow up of 25 months. The study by Einhorn et al. [15] had the longest follow-up of 10 years. The studies by Tell et al. [16] and Mercado et al. [17] each suggested that post radiation thyroid dysfunction presents between 14-18 months and hence, 1-2 years of follow up is required to adequately diagnose post radiation thyroid dysfunction. In our study, 58.7% were treated with chemoradiation, while 41.3% were treated with radiation alone. In the study conducted by Murthy et al. [18] 84.29% patients were treated with chemoradiation and 15.71% were treated with radiation alone. In our study, 35 (94.6%) patients received weekly Inj. Cisplatin (40 mg/m2) and 1 patients received Inj. Carboplatin (AUC-2) on weekly basis in our study. In the study by Banipal et al. [19] 41.5% received Inj. Cisplatin and 5-Fluorouracil and 5.6% received Inj. Cisplatin.

In our study, we observed no significant relationship between the changes in mean T3 levels and factors such as treatment method, radiation dosage, or age group. Banipal et al. [19], found that 60.3% of their subjects experienced a decrease in mean T3 levels, with variations across different age groups. However, there was no disparity in mean T3 levels concerning the treatment method. Similarly, Chougule and Kochar [17] noted a decline in mean T3 levels midway through external beam radiation therapy (EBRT), although this change lacked statistical significance. Nonetheless, a significant drop in mean T3 levels occurred at the 6-month post-radiotherapy mark.

In another study by Nishiyama et al. [20], a reduction in mean T3 levels was observed among the hypothyroid group 12 months post-irradiation, although this change was not statistically significant.

Regarding T4 levels, our study demonstrated a decreasing trend until the 12-month follow-up, although this trend did not reach statistical significance. There was also no correlation between T4 level variations and factors like age, treatment method, or radiation dosage. In contrast, Vrabec et al. [21], found a decrease in mean T4 levels in 30.8% of their patients, with lower levels noted in the radiotherapy-only group compared to the chemoradiation group. Additionally, males exhibited higher mean T4 levels than females, and higher levels were associated with radiation doses exceeding 60Gy. However, Chogule and Kochar's study showed a non-significant decrease in mean T4 levels midway through EBRT, with significance observed only at the 6-month post-radiation point.

The incidence of radiation induced hypothyroidism in our study was 46%, with a notable increase in mean TSH levels at 3, 6, 9, and 12 months from the baseline, which was statistically significant (Table 1-5 and Figure 1). Conversely, TSH levels decreased between 9 and 12 months, likely due to levo-thyroxine administration in patients with hypothyroidism. Nishiyama et al. [20] found a significant increase in TSH levels between 3 and 6 months post-irradiation. Koc and Capoglu [22] observed a median time of 15 months for clinical hypothyroidism development and 3 months for subclinical hypothyroidism. In our study, no statistically significant correlation was found between age and mean TSH levels, nor was there a positive correlation between mean TSH levels and primary site or chemotherapy use alongside radiation therapy.

In our study, increasing age was associated with a greater risk of hypothyroidism. Around 55.2% of hypothyroid patients were in the age group 51-70 years. According to the most researchers, age does not seem to be an important factor in hypothyroidism development [23-25]. Only Tell et al. [16] found that increasing age was correlated with an increased risk of hypothyroidism. In a study by Srikantia et al. [26], 52.9% of the patients who developed clinical hypothyroidism were between the age groups of 51 to 60 years which was in line with our study.

Dose of radiation required to produce hypothyroidism is not clearly defined in literature. DeGroot [27] and Hancock et al. [9] suggested that radiation doses in the range of 3000 to 8000 rads are required to produce hypothyroidism. In the study by Grande et al. [25] the incidence of hypothyroidism was 22.4% in patients receiving <60 Gy and 56% in those receiving >60 Gy. However, other studies like Alterio et al. [23] and Tell et al. [16] did not find any correlation between treatment dose and thyroid dysfunction. In our study, it was seen that patients receiving less or equal to 60Gy, only 42.86% patients developed hypothyroidism and in the group receiving >60Gy, 46.82% developed hypothyroidism. However, this difference was not found to be statistically significant.

The incidence of hypothyroidism in the RT alone group was 38.5% and in the chemoradiation group it was 51.4%. However, this difference was not found to be statistically significant. The effect of chemotherapy on the thyroid gland, especially in conjunction with radiation is not clear. It is expected that chemotherapy, particularly concurrent chemotherapy will sensitize the thyroid gland to radiation and will increase the incidence of hypothyroidism. Hancock et al. [9], reported that chemotherapy was a significant risk factor for hypothyroidism in patients receiving radiation. On the other hand, Weissler and Berry [28], Sinard et al. [29] and Mercado et al. [17] observed no increase in the incidence of hypothyroidism in patients with head and neck carcinoma who received chemotherapy as part of the treatment.

In our study, it was seen that the mean dose to the thyroid was higher in the hypothyroid group vs the euthyroid group (48.40±16.27 vs 45.30±14.25), which was not statistically significant (p-value >0.05). In the study by Ling et al. [30] the lowest mean dose at which thyroid abnormality occurred was noted to be at 29.8 Gy. In the study by Kim et al. [14] there was a positive correlation between higher mean dose to the thyroid and thyroid dysfunction. Bhandare et al. [31], found a significant difference in the incidence of hypothyroidism between two different dose levels. When the mean thyroid gland dose was 45 Gy or more, the incidence of clinical hypothyroidism was 27% after 5 years and 39% after 10 years as compared to 21% and 21%, respectively, in case of a mean thyroid gland dose less than 45 Gy.

In our study, we found that patients with stage I, II, III and IV developed hypothyroidism with incidence of 33.33%, 54.54%, 42.10% and 52.38% respectively which was not statistically significant (p>0.05). Majority of patients with T3 and T4 developed radiation-induced hypothyroidism, with incidence rates of 45% and 60% respectively.

The radiation field of head and neck cancer is related to the tumor-node-metastasis (TNM) stage. Studies have reported that early T stage is a risk factor for radiation-induced hypothyroidism , which seemed to be controversial. Wu et al. [32] reported that radiotherapy-induced damage to the pituitary gland prohibited the response of the pituitary gland to low levels of serum thyroid hormones in patients with advanced stage (T3-4) nasopharyngeal carcinoma. Theoretically, the radiation field in patients with T3-4 nasopharyngeal carcinoma includes the skull base, resulting in a high pituitary dose and a tendency to develop central hypothyroidism. This discrepancy might have been caused by the research endpoints not including central hypothyroidism. Other studies have found no correlation between T stage and the incidence of hypothyroidism [33].

Fujiwara et al. [34] analyzed 116 patients with head and neck cancer who received 3D-CRT, and univariate analysis showed that the incidence of hypothyroidism was significantly higher in the positive cervical lymph node group. Positive lymph nodes increase the exposure volume of primary tumors and the risk of thyroid irradiation; therefore, positive lymph node status is an important factor for hypothyroidism [18]. However, Koc et al. [22] believed that there is no correlation between clinical stage and hypothyroidism, which might have been affected by some confounding factors. Attention should be paid to patients with advanced N stage during individualized follow up of thyroid function test.

In our study, the mean thyroid volume in the hypothyroid group was 11.83±7.15 cm^3 compared to 13.80±6.00 cm^3 in the euthyroid group and hypothyroidism was more common in patients with smaller thyroid volumes. This difference was not statistically significant. The study by Murthy et al showed no correlation between thyroid volume and thyroid dysfunction. Jerezeck et al. [10], showed that smaller thyroid volume was associated with a higher incidence of thyroid toxicity.

The symptoms of thyroid dysfunction may go unnoticed under the cover of other associated co-morbidities and side effects of the treatment modalities. Regular testing of thyroid function in patients undergoing radiation or chemo-radiation can help in diagnosing thyroid dysfunction at the subclinical stage, before it progresses to clinical hypothyroidism. The thyroid function tests (FT4 and TSH) should be done 3 monthly for at least 2 years and then annually lifelong to accommodate for late presentation of radiation induced hypothyroidism. Larger multi-institutional studies with longer follow-up are needed to study the morbidity associated with post radiation thyroid dysfunction further.

In conclusion, this study underscores the significant incidence of hypothyroidism in patients with head and neck cancer treated with conformal radiotherapy (RT), revealing a 46% occurrence rate at a median follow-up of 9 months. This highlights the importance of recognizing RT-induced thyroid dysfunction as a substantial side effect. The data suggest that radiation can impair thyroid function through direct parenchymal damage and vascular injury, with the extent of dysfunction influenced by radiation dose and potentially augmented by concurrent chemotherapy.

Our findings demonstrate that thyroid hormone levels (fT4) tend to decrease post-radiotherapy, though these changes often lack statistical significance. Conversely, thyroid-stimulating hormone (TSH) levels significantly increase, indicating the onset of hypothyroidism. Notably, there is no clear correlation between age, treatment method, or radiation dose and the variation in thyroid hormone levels.

Moreover, the study reveals that a higher radiation dose (>60 Gy) correlates with an increased incidence of hypothyroidism, though the specific dose threshold remains undefined. While concurrent chemotherapy might sensitize the thyroid to radiation, its precise impact on thyroid dysfunction needs further clarification.

The results emphasize the need for regular thyroid function testing in patients undergoing RT or chemoradiation to identify subclinical thyroid dysfunction early. Future research should focus on larger, multi-institutional studies with extended follow-up periods to better understand the long-term morbidity associated with post-radiation thyroid dysfunction. This would aid in developing more precise guidelines for managing and mitigating this significant treatment-related side effect.

Author Contribution Statement

Author 1: Conceptualization, literature search, Data collection, Data analysis, Manuscript drafting and editing. Author 2: Critical revision, Supervision, Final approval of the manuscript. Author 3: Supervision, Final approval of the manuscript. Author 4: Supervision, Final approval of the manuscript

Acknowledgements

General

I want to express my gratitude to Prof. (Dr.) Mushood Ghulam Nabi, my mentor, for his essential assistance, encouragement, and direction during this research project. And my wife Misbah Hameed for being a constant support and source of motivation throughout. Insightful feedback and a stimulating academic environment were provided by my friends and colleagues Dr. Ubaid Jeelani and Dr Aadil Najeed, who have been supportive throughout. Their encouragement was tremendously motivating during this journey, and their invaluable contributions were crucial in determining the direction of this article.

Scientific Approval / Student Thesis

The study was conducted as part of an approved postgraduate thesis under the Department of Radiation Oncology, Government Medical College Srinagar, Jammu and Kashmir, India

Ethical Considerations

Ethical clearance for the study was obtained from the Institutional Ethics Committee of Government Medical

College, Srinagar, Jammu and Kashmir, India

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin. 2016;66(1):7-30. https://doi.org/10.3322/caac.21332.
2. Bagal S, Budukh A, Thakur JS, Dora T, Qayyumi B, Khanna D, et al. Head and neck cancer burden in india: An analysis from published data of 37 population-based cancer registries. Ecancermedicalscience. 2023;17:1603. https://doi.org/10.3332/ecancer.2023.1603.
3. Overgaard J, Hansen HS, Jørgensen K, Hjelm Hansen M. Primary radiotherapy of larynx and pharynx carcinoma--an analysis of some factors influencing local control and survival. Int J Radiat Oncol Biol Phys. 1986;12(4):515-21. https://doi.org/10.1016/0360-3016(86)90058-1.
4. Blanchard P, Baujat B, Holostenco V, Bourredjem A, Baey C, Bourhis J, et al. Meta-analysis of chemotherapy in head and neck cancer (mach-nc): A comprehensive analysis by tumour site. Radiother Oncol. 2011;100(1):33-40. https://doi.org/10.1016/j.radonc.2011.05.036.
5. Marta GN, Silva V, de Andrade Carvalho H, de Arruda FF, Hanna SA, Gadia R, et al. Intensity-modulated radiation therapy for head and neck cancer: Systematic review and meta-analysis. Radiother Oncol. 2014;110(1):9-15. https://doi.org/10.1016/j.radonc.2013.11.010.
6. Nutting CM, Morden JP, Harrington KJ, Urbano TG, Bhide SA, Clark C, et al. Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (parsport): A phase 3 multicentre randomised controlled trial. Lancet Oncol. 2011;12(2):127-36. https://doi.org/10.1016/s1470-2045(10)70290-4.
7. Bertelsen A, Hansen CR, Johansen J, Brink C. Single arc volumetric modulated arc therapy of head and neck cancer. Radiother Oncol. 2010;95(2):142-8. https://doi.org/10.1016/j.radonc.2010.01.011.
8. Soberman N, Leonidas JC, Cherrick I, Schiff R, Karayalcin G. Sonographic abnormalities of the thyroid gland in long term survivors of hodgkin disease. Pediatr Radiol. 1991;21(4):250-3. https://doi.org/10.1007/bf02018615.
9. Hancock SL, McDougall IR, Constine LS. Thyroid abnormalities after therapeutic external radiation. Int J Radiat Oncol Biol Phys. 1995;31(5):1165-70. https://doi.org/10.1016/0360-3016(95)00019-u.
10. Jereczek-Fossa BA, Alterio D, Jassem J, Gibelli B, Tradati N, Orecchia R. Radiotherapy-induced thyroid disorders. Cancer Treat Rev. 2004;30(4):369-84. https://doi.org/10.1016/j.ctrv.2003.12.003.
11. Rubin P, Casarett GW. Clinical radiation pathology as applied to curative radiotherapy. Cancer. 1968;22(4):767-78. https://doi.org/10.1002/1097-0142(196810)22:4<767::aid-cncr2820220412>3.0.co;2-7.
12. Emami B, Lyman J, Brown A, Coia L, Goitein M, Munzenrider JE, et al. Tolerance of normal tissue to therapeutic irradiation. Int J Radiat Oncol Biol Phys. 1991;21(1):109-22. https://doi.org/10.1016/0360-3016(91)90171-y.
13. Kehwar TS. Analytical approach to estimate normal tissue complication probability using best fit of normal tissue tolerance doses into the ntcp equation of the linear quadratic model. J Cancer Res Ther. 2005;1(3):168-79. https://doi.org/10.4103/0973-1482.19597.
14. Kim MY, Yu T, Wu HG. Dose-volumetric parameters for predicting hypothyroidism after radiotherapy for head and neck cancer. Jpn J Clin Oncol. 2014;44(4):331-7. https://doi.org/10.1093/jjco/hyt235.
15. Einhorn J, Wilkholm G. Hypothyroidism after external irradiation to the thyroid region. Radiology. 1967;88(2):326-8. https://doi.org/10.1148/88.2.326.
16. Tell R, Lundell G, Nilsson B, Sjödin H, Lewin F, Lewensohn R. Long-term incidence of hypothyroidism after radiotherapy in patients with head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2004;60(2):395-400. https://doi.org/10.1016/j.ijrobp.2004.03.020.
17. Mercado G, Adelstein DJ, Saxton JP, Secic M, Larto MA, Lavertu P. Hypothyroidism: A frequent event after radiotherapy and after radiotherapy with chemotherapy for patients with head and neck carcinoma. Cancer. 2001;92(11):2892-7. https://doi.org/10.1002/1097-0142(20011201)92:11<2892::aid-cncr10134>3.0.co;2-t.
18. Murthy V, Narang K, Ghosh-Laskar S, Gupta T, Budrukkar A, Agrawal JP. Hypothyroidism after 3-dimensional conformal radiotherapy and intensity-modulated radiotherapy for head and neck cancers: Prospective data from 2 randomized controlled trials. Head Neck. 2014;36(11):1573-80. https://doi.org/10.1002/hed.23482.
19. Banipal R, Mahajan MK, Uppal B, John M. Thyroid diseases as a sequelae following treatment of head and neck cancer. Indian J Cancer. 2011;48(2):194-8. https://doi.org/10.4103/0019-509x.82886.
20. Nishiyama K, Kozuka T, Higashihara T, Miyauchi K, Okagawa K. Acute radiation thyroiditis. Int J Radiat Oncol Biol Phys. 1996;36(5):1221-4. https://doi.org/10.1016/s0360-3016(96)00480-4.
21. Vrabec DP, Heffron TJ. Hypothyroidism following treatment for head and neck cancer. Ann Otol Rhinol Laryngol. 1981;90(5 Pt 1):449-53. https://doi.org/10.1177/000348948109000506.
22. Koc M, Capoglu I. Thyroid dysfunction in patients treated with radiotherapy for neck. Am J Clin Oncol. 2009;32(2):150-3. https://doi.org/10.1097/COC.0b013e3181845517.
23. Alterio D, Jereczek-Fossa BA, Franchi B, D'Onofrio A, Piazzi V, Rondi E, et al. Thyroid disorders in patients treated with radiotherapy for head-and-neck cancer: A retrospective analysis of seventy-three patients. Int J Radiat Oncol Biol Phys. 2007;67(1):144-50. https://doi.org/10.1016/j.ijrobp.2006.08.051.
24. Posner MR, Ervin TJ, Miller D, Fabian RL, Norris CM, Jr., Weichselbaum RR, et al. Incidence of hypothyroidism following multimodality treatment for advanced squamous cell cancer of the head and neck. Laryngoscope. 1984;94(4):451-54. https://doi.org/10.1288/00005537-198404000-00002.
25. Grande C. Hypothyroidism following radiotherapy for head and neck cancer: Multivariate analysis of risk factors. Radiother Oncol. 1992;25(1):31-6. https://doi.org/10.1016/0167-8140(92)90192-w.
26. Srikantia N, Rishi KS, Janaki MG, Bilimagga RS, Ponni A, Rajeev AG, et al. How common is hypothyroidism after external radiotherapy to neck in head and neck cancer patients? Indian J Med Paediatr Oncol. 2011;32(3):143-8. https://doi.org/10.4103/0971-5851.92813.
27. DeGroot LJ. Radiation and thyroid disease. Baillieres Clin Endocrinol Metab. 1988;2(3):777-91. https://doi.

org/10.1016/s0950-351x(88)80065-x.
28. Weissler MC, Berry BW. Thyroid-stimulating hormone levels after radiotherapy and combined therapy for head and neck cancer. Head Neck. 1991;13(5):420-3. https://doi.org/10.1002/hed.2880130508.
29. Sinard RJ, Tobin EJ, Mazzaferri EL, Hodgson SE, Young DC, Kunz AL, et al. Hypothyroidism after treatment for nonthyroid head and neck cancer. Arch Otolaryngol Head Neck Surg. 2000;126(5):652-7. https://doi.org/10.1001/archotol.126.5.652.
30. Ling S, Bhatt AD, Brown NV, Nguyen P, Sipos JA, Chakravarti A, et al. Correlative study of dose to thyroid and incidence of subsequent dysfunction after head and neck radiation. Head Neck. 2017;39(3):548-54. https://doi.org/10.1002/hed.24643.
31. Bhandare N, Kennedy L, Malyapa RS, Morris CG, Mendenhall WM. Primary and central hypothyroidism after radiotherapy for head-and-neck tumors. Int J Radiat Oncol Biol Phys. 2007;68(4):1131-9. https://doi.org/10.1016/j.ijrobp.2007.01.029.
32. Wu YH, Wang HM, Chen HH, Lin CY, Chen EY, Fan KH, et al. Hypothyroidism after radiotherapy for nasopharyngeal cancer patients. Int J Radiat Oncol Biol Phys. 2010;76(4):1133-9. https://doi.org/10.1016/j.ijrobp.2009.03.011.
33. Xu Y, Shao Z, Tang T, Liu G, Yuanhu Y, Wang J, et al. A dosimetric study on radiation-induced hypothyroidism following intensity-modulated radiotherapy in patients with nasopharyngeal carcinoma. Oncol Lett. 2018;16. https://doi.org/10.3892/ol.2018.9332.
34. Fujiwara M, Kamikonya N, Odawara S, Suzuki H, Niwa Y, Takada Y, et al. The threshold of hypothyroidism after radiation therapy for head and neck cancer: A retrospective analysis of 116 cases. J Radiat Res. 2015;56(3):577-82. https://doi.org/10.1093/jrr/rrv006.