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# PROSPECTIVE STUDY OF THYROID DYSFUNCTION IN POST RADIOTHERAPY PATIENTS WITH HEAD AND NECK CANCERS

**Dr. Manish Kumar Chaturvedi[1], Dr. Rameshwaram Sharma[2], Dr. Rohitashwa Dana[3], Dr. Prashant Dadhich,[4] Dr. Pawan Kumar[5], Dr. Subhash Bairwa[6], Dr. Narendra Gupta[7]**

Radiation Oncology Department, S M S Medical College, Jaipur, Rajasthan

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**Corresponding author:** Dr. Rameshwaram Sharma
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**Abstract**

Background: The purpose of our study is to identify the incidence of hypothyroidism following radiotherapy in head and neck cancer patients in Rajasthan India and to assess the time period for the development of hypothyroidism for early treatment to reduce hypothyroid related morbidity and mortality.

Methods: A prospective study conducted in Department of Radiation Oncology, S.M.S Medical College and attached group of hospital, Jaipur, Rajasthan. with 50 patients of histopathologically proven head and neck cancer receiving external beam to whole neck on telecobalt.

Results: The patients were followed up for a period of six months. 7 (14%) patients were found to have hypothyroidism which was strongly significant with the p value of 0.02.

Conclusion: We concluded that thyroid function tests should be made routine prior RT and during follow up period as early as 6 months and carried out lifelong.

Keywords: Thyroid function test, Head neck cancer, Follow-up.

## Introduction

Head-neck cancers affect the upper aerodigestive tract and are one of the most common cancers worldwide.[1] Head-neck cancers are the second most common cancers in the Indian population and 77,000 cases diagnosed per year.[2] While smoked tobacco and alcohol are the major causative factors for head-neck cancers worldwide, smokeless tobacco, betel nut, and Epstein–Barr virus are etiological agents responsible for it in the Asian population.[3] The management of head-neck cancer requires a multimodality concept and multidisciplinary approach which include radiotherapy, chemotherapy, surgery, and a combination of these. In the management of head neck cancer patients, radiotherapy is the one of the most important curative approaches, besides surgery.

Majority of head-neck cancers are loco-regionally advanced at the time of diagnosis. Hence, the radiotherapy treatment field covers the primary site of the tumor and whole neck including the thyroid gland. The thyroid gland is situated in an anterior part of the neck in front of the trachea and secretes the principal hormones thyroxine (T4) and triiodothyronine. The thyroid gland maintains the level of metabolism in the tissues that is optimal for their normal functioning. Hypothyroidism is the most common clinical delayed effect of post-radiotherapy head-neck cancer patients. Hypothyroidism may be clinical and subclinical. Clinical hypothyroidism is characterized by low free T4 and high thyroid stimulating hormone (TSH), and subclinical hypothyroidism is characterized by normal free T4 and high TSH. Subclinical hypothyroidism is also called compensated hypothyroidism. In the majority of cases, subclinical hypothyroidism progresses to clinical hypothyroidism.[4]

The mechanism of radiation-induced hypothyroidism is that radiation causes both microvascular and macrovascular damage, directly, in and around the thyroid gland and it causes tissue hypoxemia and nutrientpoor environment causes in a reduced synthetic and secretory capacity of the gland itself. Radiofibrosis of the gland's capsule may also inhibit compensatory hypertrophy in this situation. Progression to clinical hypothyroidism occurs at a rate of about 5–20% per year. Symptoms of hypothyroidism are weakness and fatigue, dry skin, feeling cold, hair loss, difficulty in concentrating and poor memory, neuropsychiatry disorder, weight gain despite poor appetite, pleural and pericardial effusion, and atherosclerosis. Early diagnosis and proper treatment reduce the rate of morbidity and mortality.[5]

The effect may be clinical hypothyroidism, with high thyroid –stimulating hormone (TSH) and low thyroxine (T4)

and the presence of clinical symptoms or sub clinical hypothyroidism, with high TSH and normal T4 level with no noticeable symptoms by the patient. Symptoms include fatigue, cold intolerance, weight gain, skin dryness, slowed mentation, depression, pleural and pericardial effusions, decreased gastrointestinal motility, congestive heart failure and acceleration of atherosclerosis .Sub clinical hypothyroidism evolves to clinical hypothyroidism at the rate of about 5 to 20% per year.

Thus, as Radiation induced hypothyroidism will markedly influence the quality of life, hence emphasizing the need for thyroid function test during the follow up.

## Material and Methods

A prospective study conducted in Department of Radiation Oncology, S.M.S Medical College and attached group of hospital, Jaipur, Rajasthan. with 50 patients of histopathologically proven head and neck cancer receiving external beam to whole neck on telecobalt.

Inclusion criteria

- Patients of any age , both sexs receiving external beam radiotherapy to the neck
- All patients had normal thyroid function test before RT.

Exclusion criteria

- Prior radiotherapy to head and neck ,recurrent disease, previous history of thyroid surgery
- Pre existing thyroid disease.

Thyroid function test was prospectively evaluated by measuring TSH (normal range,0.4 – 4.20micro IU/ml),T4(normal range,4.8-11.6n g / ml),T3(normal range,0.5-1.85ng/ml)before start of RT and periodically after completion of RT at 3 weeks , 3 months and 6 months.

Total T4 and T3 estimation was done using the Radioimmunoassay kits and TSH estimation was done using immunoradiometric assay.

Patients were treated with Cobalt 60 teletherapy unit with conventional fractionation of 1.8 to 2 Gy/Fr/day for 5 days a week. The treatment portals included the primary tumor with margin and the whole neck. For primary and the upper neck with two lateral portals and lower neck with separate central portal. The treatment intent was only radical radiotherapy with or without concurrent chemotherapy with weekly cisplatin at 40 mg/m3 of body surface area.

## Statistical Methods

Results were presented in number, percentage and mean. Statistical test is applied for final statistical association using EPI-Info software.

## Results

**Table 1:** Socio-demographic variable

| | |
|---|---|
| Mean age in Yrs | 54.23±8.35 Yrs (18-76 Yrs) |
| Sex (M:F) | 42:8 |
| Hindu : Muslim | 46:4 |
| Rural : Urban | 29:21 |

Most patients were hindu male age range 18 to 76 Yrs.

**Table 2:** Incidence of hypothyroidism according to primary site lesion

| Primary site lesion | Hypothyroidism present | Hypothyroidism absent | Total | p-value |
|---|---|---|---|---|
| Oral cavity Ca | 0 | 8 | 8 | 0.3 |
| Oropharynx Ca | 0 | 7 | 7 | 0.3 |
| Supra glottic Ca | 0 | 13 | 13 | 0.3 |
| Glottic Ca | 4 | 8 | 12 | 0.23 |
| Hypopharyngeal Ca | 3 | 7 | 10 | 0.12 |
| Total | 7 | 43 | 50 | |

**Table 3:** Occurrence of hypothyroidism at follow-up

| Outcome | Before RT | 6 weeks after RT | 3 months after RT | 6 months after RT |
|---|---|---|---|---|
| Normal | 50 | 50 | 50 | 43 |
| Hypothyroidism | 0 | 0 | 0 | 7 |

The patients were followed up for a period of six months to determine the occurrence of sub clinical hypothyroidism. 7 (14%) patients were found to have hypothyroidism which was strongly significant with the p value of 0.02.

## Discussion

Hypothyroidism after Radiotherapy for Head and Neck cancer may adversely affect the quality of life of cancer survivors therefore the National Comprehensive Cancer Network (NCCN) recommends that thyroid function tests should be repeated every 6–12 months after RT for neck. But the clinicians often fail to assess routine thyroid function test before and after RT.

First case of hypothyroidism was reported in 1961 by Felix et al, in a patient of laryngeal carcinoma after six years of treatment with external Radiotherapy.[6] 41 patients of carcinoma larynx and hypopharynx treated with RT were followed up for ten years by Einhorn and Wikholm and noted 7.3%of hypothyroidism .Weissler and Berry reported hypothyroidism after RT in 57% of his patients, similarly Leining et.al reported hypothyroidism in 26% of his patients[7,8]

In a study by Mercado *et al.,*with a median follow up of 4.4 years, reported hypothyroidism after radiotherapy in 48% of patients[9]. The documented incidence of hypothyroidism after RT varies between 3% and 44%. Most investigators

have reported an incidence of 20-30% of hypothyroidism after radiotherapy.

In majority of cancers,the primary site was hypopharynx. The primary site of the tumor was not a significant factor. The primary site varies in literature. According to Aich et al study, majority of cancers were seemed to arise from the Larynx (49%).[10]

Several mechanisms of injury to the thyroid have been proposed ranging from vascular or immunologically mediated damage to prevention of cell division leading to direct follicular destruction of the thyroid gland. Fajardo et al[11] have stated that damage to endothelial cells in thyroid capillary networks may be an important mechanism in both early and delayed radiation damage. Hellman et al, has reported that acute effects of RT depends on the balance between cell killing and compensatory replication of stem and proliferative cells. The development of late effects is due to the limited proliferative capacity of the stem cells affected by RT.

In our study, the follow-up period was 6 months post-RT, which is lower than the majority of studies. Tell et al and Turner et al had a mean follow up of 36 months and 21 months respectively.

In our study the incident rate is high when compared to other studies. The documented incidence of hypothyroidism after RT varies between 3% and 44%.

## Conclusion

We concluded that thyroid function tests should be made routine prior RT and during follow up period as early as 6 months and carried out lifelong.

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