

## COMPARATIVE ANALYSIS OF EFFECT OF CONVENTIONAL RADIOTHERAPY VERSUS CONCURRENT CHEMORADIOTHERAPY AFTER EXTERNAL BEAM RADIOTHERAPY ON THYROID GLAND IN HEAD AND NECK CARCINOMA PATIENTS AT A TERTIARY CARE HOSPITAL

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### Abstract

**Background:** Radiotherapy for patients with head and neck cancer is extremely complex and has evolved greatly in the past decade. The present study was conducted to compare the effect of conventional radiotherapy versus concurrent chemoradiotherapy on the thyroid gland after external beam radiotherapy in head-and-neck carcinoma. **Materials & Methods:** Total 100 patients were enrolled and randomized into two treatment arms. Group 1: patients received concurrent chemoradiation with injection cisplatin 35 mg/m<sup>2</sup> intravenous weekly along with radiotherapy Group 2: patients received conventional radiotherapy alone. In both arms, thyroid function test was done by radioimmuno assay method. **Results:** In the present study, a total of 100 patients of head-and-neck carcinoma were randomized in two arms. In both groups, 88% were males and 12% were females. In both groups, maximum patients were of age group 51-60 years. In group 1, a total of 62% patients developed acute hyperthyroidism and in group 2, total 68% patients developed acute hyperthyroidism. In group 1, a total of 92% patients developed Hypothyroidism and in group 2, total 22% patients developed Hypothyroidism. **Conclusion:** The study concluded that patients who received concurrent chemoradiation with injection cisplatin had developed hyperthyroidism more while patients who received conventional radiotherapy alone developed Hypothyroidism more.

## INTRODUCTION

Head and neck cancer comprises a heterogeneous group of tumors arising from the upper aerodigestive tract, paranasal sinuses, and salivary and thyroid glands. The optimal management of head and neck cancer requires a multidisciplinary approach. Surgery and radiotherapy are the major treatment modalities.<sup>[1]</sup> Thyroid hypofunction is a common side effect after such irradiation and is reported in the literature for over 40 years, with figures reaching up to 50% of irradiated patients in some works.<sup>[2]</sup> EBRT to head-and-neck region where radiation portal invariably includes thyroid gland has acute and late effect on thyroid function. During the radiation period, hyperfunction of thyroid occurs, and levels of thyroid-stimulating hormone (TSH) exhibit two phases: a significant decrease during radiotherapy (thyroxic phase) and an increase after radiotherapy

(hypothyroid phase). At higher dose levels, functional changes and thyroiditis become more prevalent during radiotherapy and this is usually transient. Increases in thyroid hormones are subtle during radiotherapy. Symptomatic hyperfunction of thyroid requires symptomatic treatment in some patients.<sup>[3]</sup> The most common clinical late effect of thyroid gland irradiation in patients exposed to therapeutic doses to the neck is hypothyroidism. This effect may be clinically overt (clinical hypothyroidism) characterized by low free T4 and high TSH or subclinical (biochemical or compensated hypothyroidism) with normal free T4 and high TSH. In the majority of cases, subclinical hypothyroidism evolves to clinical hypothyroidism. Progression to clinical hypothyroidism occurs at a rate of about 5%–20% per year.<sup>[4]</sup> The present study was conducted to compare the effect of conventional radiotherapy versus concurrent chemoradiotherapy

on the thyroid gland after external beam radiotherapy in head-and-neck carcinoma.

## MATERIALS AND METHODS

The study was conducted on patients of carcinoma of head-and-neck region, attending the Department of Radiation Oncology, Government Medical College, Haldwani, Uttarakhand, India. Before the commencement of the study ethical approval was taken from the ethical committee of the institute and informed consent was taken from the patient after explaining the study. Patients who were histopathologically confirmed squamous cell carcinoma of head-and-neck region, surgically resected confirmed case of squamous cell carcinoma of head-and-neck region, Karnofsky performance scale  $\geq 70$ , Preradiation normal thyroid function test or patient having no previous thyroid dysfunction, Patient did not receive any previous oncological treatment were included in the study. Total 100 patients were enrolled and randomized into two treatment arms.

- Group 1: Total 50 patients received concurrent chemoradiation with injection cisplatin 35 mg/m<sup>2</sup> intravenous weekly along with radiotherapy
  - Group 2: Total 50 patients received conventional radiotherapy alone. In both the groups, all patients had received radiation dose of 60–70 Gy/30–35 fractions at the rate 2 Gy per fraction with 5 fractions per week in 6–7 weeks.
- In both arms, thyroid function test was done by radioimmune assay method; it included serum TSH,

serum T4, and serum T3 levels. First, baseline thyroid function test and ultrasonography of neck along with thoroughly clinical evaluation were done for every patient and these investigations were repeated in middle of radiotherapy treatment (after 17 #), at the end of radiotherapy treatment, 3 months after completion of radiotherapy, and after that, at every 3rd-month follow-up to determine the late changes in thyroid function and echotexture after radiotherapy and concurrent chemoradiotherapy. Individual patient's records were maintained. For statistical analysis, data was collected and entered into the Microsoft Excel spreadsheet. Categorical variables were described as frequency and proportion. Continuous variables were described as mean  $\pm$  standard deviation. We compared proportions using Chi-square test and Fisher's exact test as and when required. The means in the two groups were compared using Student's t-test.  $P < 0.05$  was considered statistically significant.

## RESULTS

In the present study, a total of 100 patients of head-and-neck carcinoma were randomized in two arms. In both groups, 88% were males and 12% were females. In both groups, maximum patients were of age group 51-60 years.

In group 1, total 62% patients developed acute hyperthyroidism and in group 2, total 68% patients developed acute hyperthyroidism.

In group 1, total 92% patients developed Hypothyroidism and in group 2, total 22% patients developed Hypothyroidism.

**Table 1: Demographic characteristics**

Variable	Group 1	Group 2
<b>Gender</b>		
Male	44(88%)	44(88%)
Female	6(12%)	6(12%)
<b>Age group</b>		
20-30	4(8%)	2(4%)
31-40	8(16%)	1(2%)
41-50	14(28%)	10(20%)
51-60	18(36%)	21(42%)
61-70	6(12%)	16(32%)

**Table 2: Radiation Induced Hyperthyroidism**

Radiation Induced Hyperthyroidism	Group 1	Group 2
Acute hyperthyroidism	31(62%)	34(68%)
Normal	19(38%)	16(32%)

**Table 3: Radiation-induced Hypothyroidism**

Radiation Induced Hypothyroidism	Group 1	Group 2
Normal	4(8%)	39(78%)
Hypothyroidism	46(92%)	11(22%)

## DISCUSSION

Radiation-induced side effects can be divided into four groups on the basis of the timing of onset: acute (during treatment), subacute (within weeks to

months), delayed onset (within months to years), and very delayed onset (after several years). Knowledge of the RT planning is essential for the radiologist for accurate interpretation of posttreatment imaging and to avoid pitfalls.<sup>[5]</sup>

In the present study, a total of 100 patients of head-and-neck carcinoma were randomized in two arms. In both groups, 88% were males and 12% were females. In both groups, maximum patients were of age group 51-60 years. In group 1, total 62% patients developed acute hyperthyroidism and in group 2, total 68% patients developed acute hyperthyroidism. In group 1, total 92% patients developed Hypothyroidism and in group 2, total 22% patients developed Hypothyroidism. An incidence of 30% to 60% hypothyroidism in patients treated with IMRT has been reported in the literature.<sup>[6-8]</sup>

Thyroid gland changes related to RT for head and neck cancers in sites other than the thyroid include hormonal deficiency, benign adenoma, multinodular goiter, and thyroid cancer. The most common clinical consequence of exposure to therapeutic doses of radiation to the neck region is hypothyroidism, which usually develops after a median interval of 1.4–1.8 years.<sup>[9,10]</sup> It is believed that thyroid adverse effects occur by vascular and parenchymal damage and autoimmune and inflammatory reactions.<sup>[11]</sup>

Liening *et al.* divided their patients into the following three groups according to the therapy: RT alone, surgery in combination with RT, and thyroid-involving surgery and RT. They found an elevated TSH in 6%, 28%, and 65% patients, respectively.<sup>[12]</sup>

A study by Gupta S *et al* found that, in arm I, total 60% patients developed acute hyperthyroidism while in arm II, 68.75% patients developed acute hyperthyroidism. A total of 18.36% of patients were found to have subclinical hypothyroidism. At the 9th month of follow-up, 55 out of 98 patients (56.12%) developed hypothyroidism. Among 55 patients, 37 were having clinical hypothyroidism while 18 patients were having subclinical hypothyroidism ( $P \leq 0.0001$ ). Maximum number of patients, i.e. 26/98 (47.27%) developing hypothyroidism were between 51 and 60 years of age group. Addition of surgery and chemotherapy had shown no difference in thyroid dysfunction.<sup>[13]</sup>

## CONCLUSION

The study concluded that patients who received concurrent chemoradiation with injection cisplatin had developed hyperthyroidism more while patients

who received conventional radiotherapy alone developed hypothyroidism more.

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