

## Original Research

### Prevalence of Radiotherapy Induced Oral Mucositis in Head and Neck Cancer Patients

Raj Kumar Nirban<sup>1\*</sup>, Rajesh Kumar<sup>2</sup>, Sitaram Mahariya<sup>2</sup>, Kamlesh Harsh<sup>3</sup>, Neeti Sharma<sup>5</sup>

<sup>1</sup>Senior specialist, Department of Radiotherapy, SP Medical College, Bikaner, Rajasthan, India

<sup>2</sup>Junior specialist, Department of Radiotherapy, SP Medical College, Bikaner, Rajasthan, India

<sup>3</sup>Associate professor, Department of Radiotherapy, SP Medical College, Bikaner, Rajasthan, India

<sup>4</sup>Senior professor, Department of Radiotherapy, SP Medical College, Bikaner, Rajasthan, India

#### ABSTRACT:

**INTRODUCTION:** Mucositis is a common complication of cancer therapy, which significantly affects the mucosa. The severity depends on a variety of factors, including the dose of medication, dose interval, the volume of treated tissue and the type of radiation. **AIM:** To investigate the prevalence of radiation-induced OM and report its associated factors. **MATERIAL AND METHODS:** A cross-sectional retrospective study was conducted by involving data patients with head and neck cancer. Data were collected from the medical records of all patients submitted to radiotherapy for the treatment of head and neck cancer from last 5 years duration. **RESULTS:** A total of 200 medical records of patients submitted to radiotherapy for the treatment of head and neck cancer were evaluated. The prevalence of RIM in the overall sample was 73% (n=146) and was found to be higher in males (76%) in comparison to females. The mean time to the onset of RIM was 15.6±1.9 days. The frequencies of osteoradionecrosis and oral candidiasis were 6% and 18%, respectively. The observed risk factors that were significantly associated with OM were osteoradionecrosis, chemotherapy, and radiation dose. **CONCLUSION:** Radiation-induced oral mucositis affects the quality of life of the patients and the family concerned. The management of oral mucositis remains a challenge. Our results suggest that adequate oral care prior to treatment for head and neck cancer is necessary.

**KEY WORDS:** Radiation induced Mucositis, head and neck cancer, risk factors

Received: 14, January 2021

Accepted: 25 February, 2021

**Corresponding Author:** Dr. Raj Kumar Nirban, Senior specialist, Department of Radiotherapy, SP Medical College, Bikaner, Rajasthan, India

**This article may be cited as:** Nirban RK, Kumar R, Mahariya S, Harsh K, Sharma N. Prevalence of Radiotherapy Induced Oral Mucositis in Head and Neck Cancer Patients. J Adv Med Dent Scie Res 2021;9(3):116-119.

#### INTRODUCTION:

Mucositis is a common complication of cancer therapy, which significantly affects the mucosa. Oral mucositis refers to the oral erythematous and ulcerative lesions commonly observed in patients undergoing cancer therapy. Clinically symptoms include severe pain as well as difficulties in eating and performing oral hygiene, thereby compromising quality of life and potentially leading to suspension of cancer treatment, which increases the risk of death. The oral regions most affected by Radiation induced Mucositis (RIM) are the floor of the mouth, lateral edge of the tongue, buccal mucosa and soft palate<sup>1</sup>.

The pathogenesis of oral mucositis (OM) is complex and related to xerostomia, which is a consequence of the impairment of the salivary glands caused by

radiation. OM may occur during or after treatment. The initial presentation is erythema followed by white desquamating plaques, which are painful when touched. Epithelial crusting and a fibrin exudate result in a pseudomembrane and ulceration, which is the more pronounced form of mucositis. Patients invariably complain of pain. Exposure of the richly innervated underlying stromal connective tissue due to loss of epithelial cells is found in the most severe form of mucositis;<sup>16</sup> this condition is usually seen 5 to 7 days following medication<sup>2,3</sup>.

Patients for head and neck cancer radiation therapy receive approximately 200 cGy daily dose of radiation, five days per week, for five to seven continuous weeks. Radiation-induced oral mucositis occurs in up to 80% of head and neck cancer

irradiated patients and reaches up to 100% in patients with altered fractionation head and neck cancer. Patients receiving cumulative radiation doses >5000 cGy, hyperfractionation with dose escalation, accelerated radiation schedules, and/or concomitant chemo-RT [CCRT] are more likely to develop RIM lesions.

The severity depends on a variety of factors, including the dose of medication, dose interval, the volume of treated tissue and the type of radiation. Other factors are prior exposure to chemotherapy, concomitant chemotherapy, and systemic diseases such as diabetes mellitus or vascular conditions<sup>4</sup>. In most patients healing occurs two or three weeks after the end of conventionally fractionated radiotherapy<sup>5</sup>.

Despite its ubiquitous presence, the clinical impact and associated factors has not been well-predicated. Thus, the aim of the present study was to investigate the prevalence of radiation-induced OM and report its associated factors.

**MATERIAL AND METHODS:**

A cross-sectional retrospective study was conducted among head and neck cancer patients. Data were collected from the medical records of all patients submitted to radiotherapy for the treatment of head and neck cancer from last 5 years duration.

All the records were examined for the following variables: Age, sex, type of malignancy, location of tumor, history of alcohol and tobacco use, radiation dose, occurrence of OM and tooth extractions before and after radiotherapy. Those patients who had

reported underlying diabetes-mellitus, history of allergy to Aloe-vera, on immunosuppressant's and HIV-positive were excluded from the study. The investigation only included information from medical records that were correctly filled out and had the patient's authorization in the form of a signed statement of informed consent.

**STATISTICAL ANALYSIS:**

The data were analyzed using descriptive and inferential statistics with the aid of the Statistical Package for the Social Sciences (SPSS, version 21.0; USA). After the descriptive analysis, regression analysis was performed to determine associations between the dependent variable (OM) and the independent variables. P<0.05 was considered as statistically significant.

**RESULTS:**

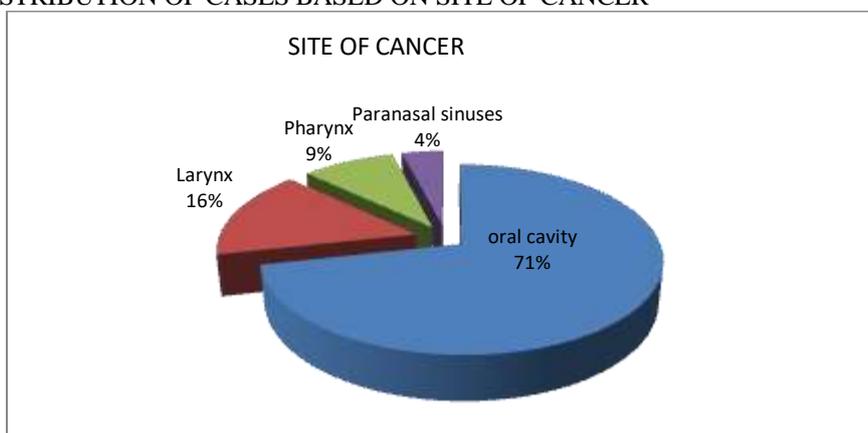
In the present study, a total of 200 medical records of patients submitted to radiotherapy for the treatment of head and neck cancer were evaluated. We observed that among the study population 170 (85%) were males and 30 (15 %) were females. Most common age group was 45-60 years with a mean age of 54.31±8.2 years. The observed mean body weight of the study population was 71.8 kg. 184 (92%) of the patients had a history of tobacco use (both in smoking ad smokeless forms). None of the respondents were smoking or using tobacco during the treatment course. 61 (30.5%) of the patients were hypertensive/CAD.

TABLE 1: DEMOGRAPHIC VARIABLES OF STUDY POPULATION:

PATIENT CHARACRTERISCTICS	NUMBER OF PATIENTS	PERCENT
<b>GENDER</b>		
MALE	170	85%
FEMALE	30	15%
MEAN AGE	54.31±8.2 years	
MEAN BODY WEIGHT	71.8 kg	
HISTORY OF TOBACCO USE	184	92%
COMORBIDITY:HYPERTENSION	61	30.5%

Squamous cell carcinoma was the most frequent type of tumor (76; n=153) and the oral cavity was the most frequent location (143;71%), followed larynx (31;16%), pharynx (18;9%) and paranasal sinuses (8;4%). Maximum number of tumors categorised as T2 (40%), followed by T3 (25%) and T4 (15%) and T1 (10%).

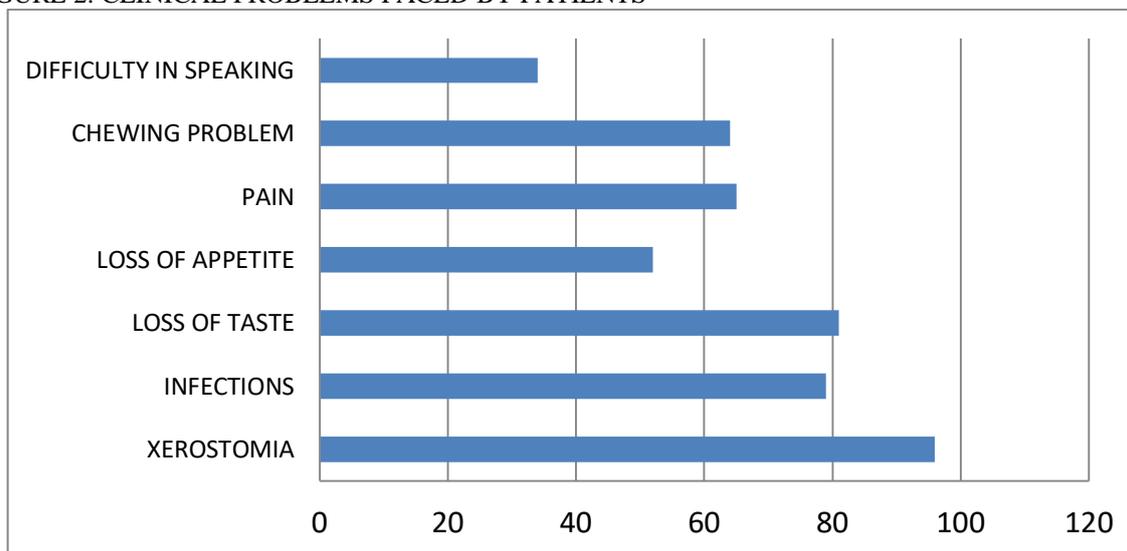
FIGURE 1: DISTRIBUTION OF CASES BASED ON SITE OF CANCER



Majority of the respondents had received a mean radiation dose of 61.26Gy for 30.8 fractionation days for a total period of 5-7 weeks. The prevalence of RIM in the overall sample was 73% (n=146) and was found to be higher in males (76%) in comparison to females. The mean time to the onset of RIM was 15.6±1.9 days. The frequencies of osteoradionecrosis and oral candidiasis were 6% and 18%, respectively.

In the present study we observed other clinical problems associated with RIM included xerostomia, fungal and/or bacterial infections, loss of taste, loss of appetite, pain, eating problems which included difficulty in eating hard food, mastication, eating/drinking food/fluids. Difficulty in speaking was also observed due to xerostomia.

FIGURE 2: CLINICAL PROBLEMS FACED BY PATIENTS



The observed risk factors that were significantly associated with OM were osteoradionecrosis, chemotherapy, and radiation dose. The extraction of compromised teeth prior to radiotherapy was a significant protective factor in prevention against OM. Factors like gender or body weight, history of alcohol or tobacco use, tumor stage were not found to be significantly associated with severity of RIM.

**DISCUSSION:**

Radiotherapy is part of a standard treatment regime for head and neck cancer. It is performed as either an initial treatment or as a postoperative therapy. RT causes a number of adverse events, including oral mucositis, xerostomia, taste disturbance, trismus, dental caries, and osteoradionecrosis of the jaw; Oral mucositis (OM) is one of the most significant and common complications of radio/chemotherapy for the treatment of head and neck cancer. Its severity is dependent on the type of ionizing radiation, the volume of irradiated tissue, the dose per day, and cumulative dose. The oral regions most affected by OM are the floor of the mouth, lateral edge of the tongue, buccal mucosa and soft palate. An in-depth investigation of OM would provide information for better clinical management of this complication, contributing to its prevention and improving the quality of life of patients. Hence the present study was aimed to investigate the prevalence of radiation-induced OM and report its associated factors.

The prevalence of radiation-induced OM in the present study was 73%. Various studies from previous studies that from rates of incidence if OM ranged to a frequency of as high as nearly 100%<sup>6-8</sup>.

Maree, J.E., et al<sup>9</sup> reported oral mucositis was a common problem, seen in 71.7% (n = 76) of their patients. Pain was not effectively managed, as 69.8% (n = 53) of respondents experienced pain whilst only 17.1% (n = 13) reported to have used analgesics. A significant difference was found between using non-prescribed self-care measures and the duration of oral mucositis. They concluded that the management of oral mucositis remains a challenge. Failure to palliate this distressing symptom can lead to the use of potentially harmful self-care measures.

Pereira et al<sup>10</sup> in their study reported that mean prevalence of OM in the overall sample was 41.9% and was higher among males (78.2%). The following variables were significantly associated with the outcome: radiation dose; concomitant chemotherapy, oral candidiasis and osteoradionecrosis. They thus concluded that Radiation-induced OM was associated with radiation dose, concomitant chemotherapy, oral candidiasis and osteoradionecrosis. The rate of OM underscores the importance of adequate oral care prior to treatment for head and neck cancer.

Histopathologically, edema of the retepegs is noted, along with vascular changes that demonstrate a thickening of the tunica intima with concomitant reduction in the lumen size and destruction of the elastic and muscle fibers of the vessel walls. The loss

of the epithelial cells to the basement membrane exposes the underlying connective tissue stroma with its associated innervations, which, as the mucosal lesions enlarge, contributes to increasing pain. If the patient develops both severe mucositis and thrombocytopenia, oral bleeding may occur, which is very difficult to treat<sup>11</sup>.

Commonly used medication in chemotherapy includes antimetabolic drugs, such as methotrexate, which inhibit DNA synthesis and tend to produce mucositis. Similar effects are seen with alkylating agents, such as 5-fluorouracil, used frequently in the treatment of gastrointestinal tract malignant tumors. Antibiotics, such as adriamycin, may cause direct effects in the mouth, or side effects as a result of its action on accessory salivary glands. Plant alkaloids rarely cause direct derangement of the oral mucosa, but may affect the mouth as a result of their neurotoxic effects<sup>13,14</sup>.

Multiple studies have demonstrated that maintenance of good oral hygiene can reduce the severity of oral mucositis. Furthermore, oral decontamination can reduce infection of the oral cavity by opportunistic pathogens. The RTOG and MASCC/ISOO (Mucositis study group of the multinational association for supportive care in cancer and the International society of oral oncology) guidelines recommend use of a standardized oral care protocol, including brushing with a soft toothbrush, flossing, and the use of nonmedicated rinses (for example, saline or sodium bicarbonate rinses). Patients and caregivers should be educated regarding the importance of effective oral hygiene.<sup>14</sup>

#### CONCLUSION:

Radiation-induced oral mucositis affects the quality of life of the patients and the family concerned. The management of oral mucositis remains a challenge. Our results suggest that adequate oral care prior to treatment for head and neck cancer is necessary. The present day management of oral mucositis is mostly focuses on palliative and or supportive care, thus Future research for the newer drugs in the field of radiation-induced oral mucositis is a required.

#### REFERENCES:

1. Mosel DD, Bauer RL, Lynch DP and Hwang ST: Oral complications in the treatment of cancer patients. *Oral Dis* 17: 550-559, 2011.
2. Raber-Durlacher JE. Current practices for management of oral mucositis in cancer patients. *Supportive care in cancer*. 1999 Feb;7(2):71-4.
3. Hanchanale S, Adkinson L, Daniel S, Fleming M and Oxberry SG: Systematic literature review: Xerostomia in advanced cancer patients. *Support Care Cancer* 23: 881-888, 2015.
4. Parulekar W, Mackenzie R, Bjarnason G, Jordan RC. Scoring oral mucositis. *Oral oncology*. 1998 Jan 1;34(1):63-71.
5. Biswal BM, Zakaria A, Ahmad NM. Topical application of honey in the management of radiation mucositis. A preliminary study. *Supportive Care in Cancer*. 2003 Apr;11(4):242-8.
6. Feller L, Essop R, Wood NH, Khammissa RA, Chikte UM, Meyerov R, Lemmer J. Chemotherapy- and radiotherapy-induced oral mucositis: pathobiology, epidemiology and management. *SADJ*. 2010 Sep 1;65(8):372-4.
7. Nicolatou-Galitis O, Kouloulis V, Sotiropoulou-Lountou A, Dardoufas K, Polychronopoulou AP, Athanassiadou P, Kolitsi G, Kouvaris J. Oral mucositis, pain and xerostomia in 135 head and neck cancer patients receiving radiotherapy with or without chemotherapy. *The Open Cancer Journal*. 2011 Mar 31;4(1).
8. Lakhani MR. Incidence and Risk factors of Radiation induced Mucositis in Patients with Head and Neck malignancy undergoing radiotherapy: An observational study in a selected hospital in Mumbai, India.
9. Maree, J.E., Combrink, M.J., De Lange, T., Toerien, A.S. & Bedeker, M. 'Incidence, severity and management of cancer chemotherapy related oral mucositis in Eastern and Western Cape', *Health SA Gesondheid* .2012;17(1)
10. Pereira IF, Firmino RT, Meira HC, Vasconcelos BC, Noronha VR, Santos VR. Radiation-induced oral mucositis in Brazilian patients: Prevalence and associated factors. *in vivo*. 2019 Mar 1;33(2):605-9.
11. Ps SK, Balan A, Sankar A, Bose T. Radiation induced oral mucositis. *Indian J Palliat Care*. 2009 Jul;15(2):95-102. doi: 10.4103/0973-1075.58452. PMID: 20668585; PMCID: PMC2902123.
12. Sonis ST, Fazio RC, Fang L. Complicações bucais da quimioterapia do câncer. *Medicina Oral*. Rio de Janeiro: Guanabara Koogan. 1989:375-401.
13. Luiz Evaristo Ricci Volpato, Thiago Cruvinel Silva, Thaís Marchini Oliveira, Vivien Thiemy Sakai, Maria Aparecida Andrade Moreira Machado. Radiation therapy and chemotherapy-induced oral mucositis. *Brazilian Journal of Otorhinolaryngology*. 2007;73(4); 562-568,
14. McGuire DB, Correa ME, Johnson J, Wienandts P. The role of basic oral care and good clinical practice principles in the management of oral mucositis. *Support Care Cancer*. 2006;14:541-7.