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ORIGINAL ARTICLE

ASSOCIATION OF MUCOSITIS WITH VARIOUS PREDISPOSING FACTORS IN THE PATIENTS WHO UNDERWENT RADIOTHERAPY FOR HEAD AND NECK CANCERS- A HOSPITAL BASED STUDY

Pardeep Garg[1], Parveen Kaur[2], Rajesh Vashistha[3], Rupinder Singh[4], Ishu Sharma[5]

[1]Associate professor, Department of Radiotherapy, GGS Medical College Hospital, Faridkot, Punjab, India,
[2]Senior consultant and head, Department of Radiotherapy, Fortis hospital, Ludhiana, Punjab, India,
[3]Senior consultant and head, Department of Oncology, Max superspeciality hospital, Bathinda, Punjab, India,
[4]Head of dentistry, Md Oswal Cancer Treatment and Research Foundation, Ludhiana, Punjab, India,
[5]Consultant and incharge, Department of Radiotherapy, MD oswal cancer treatment and research foundation, Ludhiana

ABSTRACT:
Background-The standard treatment for patients with locally advanced head neck cancer has been surgery followed by postoperative radiotherapy. Head and neck cancers are relatively chemo-sensitive. The concomitant administration of chemotherapy and radiotherapy has been the most hopeful strategy in recent years. **Material and methods:** The study was conducted head & neck cancer patients receiving radiotherapy. Patients particulars were noted, a thorough history of the disease. Any history of addiction to smoking, alcohol, opium and tobacco consumption was taken. History of diabetes mellitus was noted. A complete physical examination with assessment of ECOG performance score, Pre treatment oral assessment, primary tumor size and regional lymph nodes was carried out for all the patients in the study and association of various factors with severity of mucositis was noted. The independent sample "t-test" was used to assess group differences for continuous variable. **Results:** 62 out 115 (53.91%) patients in the smoker group showed grade IV mucositis. Tobacco chewing was associated with mucositis grade IV in 90% patients as against 20.25% in non-tobacco chewer group (p value < 0.01). Association of grade IV mucositis was observed in 58/98 (59.18%) patients with bad ODH. In smoker group, the incidence of mucositis was more as compared to the non-smoker group and p value < 0.01 was seen suggesting of high significance. **Conclusion:** After 60 years of age group, mucositis grade IV incidence was seen to increase from 50% in below 60 year age group to 56.33%. Tobacco taken in any form by head and neck cancer patients makes them highly prone to develop grade IV mucositis
Keywords- Mucositis; Radiotherapy; Tobacco

Corresponding author: Dr. Pardeep Garg, Associate professor, Department of Radiotherapy, GGS Medical College Hospital, Faridkot, Punjab, India,

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INTRODUCTION-

5 years survival rate for mouth, tongue, oropharynx and laryngopharyngeal cancers seldom exceed 40%. Involvement of regional LN(s) is still the single most important prognostic factors for Head and Neck cancers. The standard treatment for patients with locally advanced head neck cancer has been surgery followed by postoperative radiotherapy. Head and neck cancers are relatively chemo-sensitive. The concomitant administration of chemotherapy and radiotherapy has been the most hopeful strategy in recent years. Chemotherapy given concomitantly with radiotherapy leads to a better outcome than radiotherapy alone.[1-4] The chemoradiation has produced results comparable to surgery plus adjuvant radiation, this modality is being advocated for organ preservation. Chemoradiation improves local and regional treatment results, with acceptable local toxicity and long term disease control. [5-7] The effectiveness of radiation therapy often depends on the ability to deliver an appropriate cumulative dose of radiation during a planned time frame. A definite course of radiotherapy in head and neck carcinoma extends for about 6 weeks to 8 weeks and is accompanied by its acute and late reactions, notably increased incidence of mucositis that causes substantial

pain and interfere with patient's ability to chew and swallow and worsens the patient's Quality of Life (QoL) at the same time.[8-11] The term oral mucositis and stomatitis are often used inter- changeably at the clinical level, but do not reflect identical process. Oral mucositis describes inflammation of oral mucosa resulting from chemotherapeutic agents or ionizing radiations. It typically manifests as erythema or ulcerations. Stomatitis refers to any inflammatory condition of oral tissue, including mucosa, dentition / periapices and periodontium. Stomatitis thus includes infections of oral tissue, as well as mucositis as defined above. Virtually all patients who receive radiotherapy to the head and neck area develop oral complications.

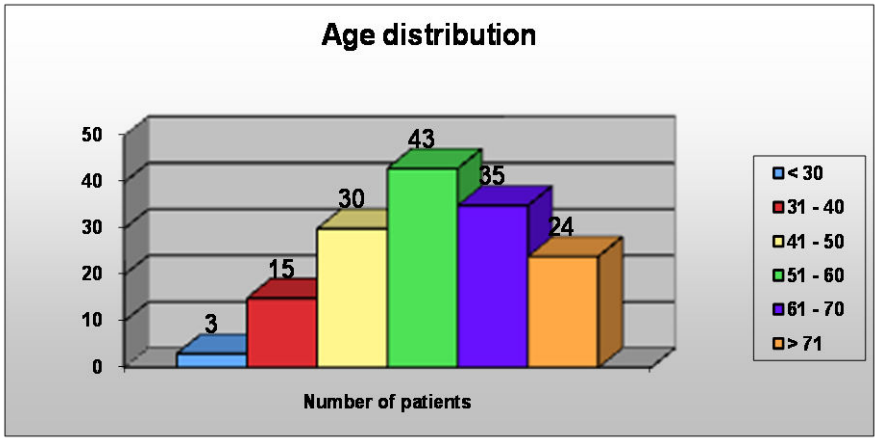
MATERIAL AND METHODS

The study is a single center prospective study conducted at Mohan Dai Oswal Cancer Treatment and Research Foundation, Ludhiana amon head & neck cancer patients receiving treatment. 150 head and neck squamous cell carcinoma (AJCC Stage I-IV) patients receiving radiation dose more than or equal to 56 gray, weekly concomitant chemoradiation in the form of Cis-platinum, Gemcitabine or Paclitaxel alternating with Gemcitabine were included in the study. A signed informed consent was obtained from the patients. Patients particulars were noted, a thorough history of the disease. Any history of addiction to smoking, alcohol, opium and tobacco consumption was taken. History of diabetes mellitus was noted. A complete physical examination with assessment of ECOG performance score, Pre treatment oral assessment, primary tumor size and regional lymph nodes was carried out for all the patients in the study.

Routine investigations like CBC, RFT, TSP, DSP, CXR-PA view, ECG were noted and ECHO was done where required. Mucositis was determined weekly while the patient was on chemo-radiation or radiation. Grading of mucositis was recorded till first (after 15 days of completion of treatment) and second follow-up (after 30 days of completion of treatment). For each group master chart were made showing all the categories and continuous variables. Results were displayed as mean ± standard deviation or percentage. The independent sample "t-test" was used to assess group differences for continuous variable

RESULTS

Median age in female was 55 years lower than found in males i.e. 58 years. Overall median age was found to be 57 years (table and graph 1). Table 2 shows association of mucositis grade IV with various predisposing factors. 62 out 115 (53.91%) patients in the smoker group showed grade IV mucositis (table 3). While seeing the association of mucositis grade IV with tobacco chewing, 16/79 (20.25%) patients in non-tobacco chewer group developed mucositis grade IV while in the tobacco chewer group mucositis was observed in 64/71(90.01%) patients (table 4). Grade IV mucositis was observed in 14/26 (53.84%) patients in opium addicts while same was observed in 66/124 (53.22%) patients in non opium addicts (table 5).
Association of grade IV mucositis was observed in 58/98 (59.18%) patients with bad ODH. Grade IV mucositis was seen in 22/52 (42.30%) patients with satisfactory ODH (table 6). 42/78 (53.84%) patients observed the grade IV mucositis in alcoholics and 38/72 (52.78%) patients in non alcoholic group (table 7). 9/14 (64.28%) diabetic patients observed the grade IV mucositis while in non diabetic group, only 71/136 patients observed the grade IV mucositis (table 8).



Graph 1: Distribution of patients according to age

Table 1: Median age of patients in the study

Median Age in study	Age (in years)
Median age (male + female)	**57**
Median age (female)	**55**
Median age (male)	**58**

Table 2: Association of mucositis grade IV with predisposing factors

	Number of patients	Grade IV
Smoker	115	**62**
Tobacco chewer	71	**64**
Opium	26	**14**
Oral Hygiene bad	98	**58**
Alcoholics	78	**42**
Diabetics	**14**	**9**

Table 3: Association of grade IV mucositis with smoking

	Number of patients	Grade IV
Smoker	115	**62 (53.91%)**
Non Smoker	**35**	**18 (51.42%)**

Table 4: Association of grade IV mucositis with tobacco chewing

	Number of patients	Grade IV
Tobacco chewer	71	**64 (90.01%)**
Non tobacco chewer	**79**	**16 (20.25%)**

Table 5: Association of grade IV mucositis with opium addiction

	Number of patients	Grade IV
Opium	26	**14 (53.84%)**
Non opium	**124**	**66 (53.22%)**

Table 6: Association of grade IV mucositis with ODH

	Number of patients	Grade IV
Oral Hygiene bad	98	**58 (59.18%)**
Oral Hygiene satisfactory	**52**	**22 (42.30%)**

Table 7: Association of grade IV mucositis with Alcohol intake

	Number of patients	Grade IV
Alcoholics	78	**42 (53.84%)**
Non alcoholics	**72**	**38 (52.78%)**

Table 8: Association of grade IV mucositis with diabetes

	Number of patients	Grade IV
Diabetics	14	**9 (64.28%)**
Non diabetics	**136**	**71 (52.20%)**

DISCUSSION-

The study was conducted with the primary aim to rule out the association of different predisposing factors with the incidence of mucositis in patients who underwent radiotherapy for head and neck cancers. All patients were treated on Theratron 780 cobalt unit with immobilization cast made for stabilization. One fraction daily was given with five days a week regimen and most of the patients complete their treatment on daily outdoor basis with admission for mucositis and weekly concomitant

chemotherapy. Smoking in any form was observed in 117 (78%) patients of the present series showing statistically significant ($p<0.01$) association with head and neck cancers. ICMR data suggests that smoking is the main etiological factor and it increases the risk of developing head and neck cancer by 5-25 folds [(12)]. Zarda consumption was observed in 70 (47%) patients. Alcohol consumption was seen in 51.33% of studied population. However no statistical significant association could be derived. Alcohol is shown to be one of the main additive factors as per ICMR data. Poor ODH was significantly associated with the head and neck cancer with p value < 0.01. ICMR data also suggest ODH as one of the causative factor [(12)].In diabetics, the prevalence of sever mucositis was more (64.28%) as compared to the non-diabetic group (52%). Statistical significance could not be drawn but diabetes was certainly leading to the higher frequency of mucositis grade IV in study. Sonis et al[11] and many others[13-16] have described the positive impact of diabetes in development of mucositis. In smoker group, the incidence of mucositis was more as compared to the non-smoker group and p value < 0.01 was seen suggesting of high significance. Various authors have described the positive impact of smoking in development of mucositis.[17-22] There is statistical significant impact of smoking in mucositis grade III/ IV development.Bad ODH was significantly associated with the development of grade IV mucositis in the present series (p value < 0.01). It has also been depicted in many studies[13,16-22] that bad ODH leads to increased incidence of grade IV mucositis as the chances of development of superimposed infection rises and healing is delayed.

Tobacco chewing was associated with mucositis grade IV in 90% patients as against 20.25% in non-tobacco chewer group (p value < 0.01). Tobacco in various forms is consumed and supposed to contain the large number of irritant compounds leading to increased chances of development of grade IV mucositis.[22]

CONCLUSION-

After 60 years of age group, mucositis grade IV incidence was seen to increase from 50% in below 60 year age group to 56.33%. Tobacco taken in any form by head and neck cancer patients makes them highly prone to develop grade IV mucositis. The severe mucositis was observed more in smokers, alcoholics, diabetics, opium addicts and patients having bad ODH. Mucositis resolves with in 4-5 week period after the completion of treatment.

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